MEDICAL BIOMETEOROLOGY

WEATHER, CLIMATE AND THE LIVING ORGANISM

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WITH 101 ILLUSTRATIONS AND 44 TABLES

DEDICATED TO MY FATHER

TO PROFESSOR WILLEM J. DE LANGEN,
whose inspiring personality and unabated interest in Biometeorological Research laid the foundation of the present book, and

TO PROFESSOR WILLIAM F. PETERSEN
and his colleagues who helped to pave the way for the modern development of biometeorology.

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S. W. TROMP

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Introduction

SIGNIFICANCE OF BIOMETEOROLOGY

Biometeorology, the science studying the influence of weather and climate on the living organism, is a young and at the same time a very old science, young by scientific standards, old if we consider the strong belief of man, from the earliest historic times to the present day, in the great influence of weather and climate on man's behaviour and happiness and on the origin of his diseases.

When the Greek and Roman civilizations were at their zenith, important political decisions were not carried into effect and war campaigns were often postponed until the weather gods had been consulted. In the Temple of the Winds at Athens in Greece a little marble octagon tower was built, the eight sides of which represent the eight principal winds in Greece. On each side is sculptured a human figure, symbolizing the character and influence on man of the particular wind it faces.

But even in the 20th century, the estimated effect of the weather upon certain future events in the Second World War was often thoroughly considered before important decisions as to those events were taken. Only the Army Chiefs and politicians who are responsible for the great decisions affecting the fate of mankind may realize how much the outcome of their decision could have been reversed by unexpected weather changes. Everybody knows how the success of an invasion fleet depends to a considerable extent on the weather conditions during the period of invasion.

In other respects as well, man is always aware of the constantly changing atmosphere in which he lives. Millions of people listen daily to radio or television weather forecasts and make their plans accordingly. No long-distance flight will be made by even the most experienced pilot without first consulting the latest weather reports relating to his route.

When snow blankets the countryside, when fog and icy road surfaces take a heavy toll of life and throw transport into confusion, the impact of the restless atmosphere upon living organisms is brought home to each one of us.

Disastrous harvests, as a result of unexpected severe night frosts after periods of warm sunny spring weather, may bring crippling losses to farmers. The same applies to a great shortage or surplus of rain in certain parts of the world and the destructive effect of cyclones or typhoons, particularly in the Western Pacific Ocean and Caribbean Sea area. Serious local economic disruptions are created almost every year in certain parts of the world as a result of abnormal weather conditions.

All this, however, is only the indirect effect of the weather and climate on man. More directly, many people know from their own experience, particularly on hot summer days and in hot humid tropical regions, how their activities and capacity to think are deeply affected by the weather and the climatic conditions under which they have to work and live. This fact was realized by the Greeks and by Hippocrates in particular, who developed a special weather calendar for the different seasons. The oldest known calendar seems to have been made by the Greek astronomer Meton in 432 B.C.

Hippocrates in his book *Airs, Waters, Places*, wrote the following interesting statements:

> "Whoever wishes to pursue properly the science of medicine must proceed thus. First he ought to consider what effects each season of the year can produce: for the seasons are not alike, but differ widely both in themselves and at their changes".
>
> "One should be especially on one's guard against the most violent changes of the seasons, and unless compelled, one should neither purge nor apply cautery or knife to the bowels, until at least ten days have passed".

The far-sightedness of Hippocrates' statements will be fully appreciated later in this book.

Reverting to our modern ways of life, it is interesting to observe that at the end of the winter in northern countries the general population often shows signs of tiredness and irritability after the long, gloomy, cold winter months. At the end of March, with sunshine increasing and the blue skies reappearing, the landscape is seen to change and most people begin to feel happy again. Yet many complain at this time of feeling tired. These phenomena, known as *winter-irritability* and *spring-tiredness*, are often denoted as merely psychological effects. However, recent physiological studies have demonstrated certain objective physiological changes in the blood of a healthy population group in winter and spring, which associate these phenomena with a physiological cause. The psychological effect is only a minor superimposed feature.

During the same period of winter-irritability in Europe many people may go skiing in the Tyrol or Switzerland, returning, tanned and healthy, to their climatologically less favoured compatriots. Here again part of their healthy state is due to psychological causes, but a considerable part is due to the stimulating effect of increased ultraviolet radiation with a particular wavelength spectrum and a general high altitude effect, which we shall discuss later.

Several research workers in the field of biometeorology go so far as to explain racial differences, and even part of the development of civilizations, on the basis of climatic differences in the past and present. Their views are supported by the present knowledge of paleontologists, who are able to explain a great number of the evolutional developments and the geographical distribution of animals and plants by the paleoclimatological changes and the distribution of climate on earth.

One of the strongest advocates of the concept of climatological influence on race and civilization is E. Huntington[1750–1757], late Research Associate in Geography in Yale University (U.S.A.). He compares the different races on earth with the trees whose yield of luscious fruit depends on racial inheritance, on cultivation of the land and on the climate. In a number of publications Huntington has defended the climatic factor. We shall look into this fascinating problem more carefully on pp. 436–447 of this book.

Another fascinating aspect of biometeorology is the possible influence of the various climates on the expression of art. The objects and light effects in paintings of N.W. European and Italian artists are clearly distinct in character, not only owing to divergencies of race, political outlook and religious persuasion, but probably also because of the differences in climatologically determined temperament and actual differences in light and shade effects surrounding the painted objects.

The people living under blue skies in sunny countries around the Mediterranean and in the Middle East, despite a lower living standard, poorer hygienic conditions and often greater prevalence of infectious diseases than most northern countries in Europe, are usually more cheerful than the majority of the northern races, who often lack the spontaneity, lightheartedness and zest of their southern brethren. On the other hand, these northern colder climates seem to give greater stimulus to the productive mental activity of man.

It is not, however, only in men and animals that we observe a sensitivity to changes in weather and climate. We likewise see the seasonal changes in the vegetable kingdom and the daily opening and closing of some flowers in response to rhythmical changes in the intensity of solar radiation and temperature.

Undoubtedly many of the examples described of the influence of weather and climate on man are partly due to the psychological effects of weather. Beautiful, sunny weather favours many pleasant human activities and tends to put people in a good humour. However, if such periods continue for a very long period, as in 1959 in W. Europe, several unpleasant physiological reactions are observed which clearly indicate that the effects of the sun cannot be explained on psychological grounds only.

It is coming to be realized more and more that weather sensitivity, known as *meteorotropism*, is not only a psychological, but also, and mainly, a true physiological phenomenon which can be explained by the known laws of physicochemistry and electrophysiology.

Unfortunately, many unscientific papers have been published in the past on this subject, both by laymen and scientists, which have done a lot of harm to this new science and undoubtedly hampered its progress during the 20th century.

The present book is an attempt to summarize what is known so far of the influence of weather and climate on the living organism, in particular man, a field of study so vast that it is now beyond the competence of anyone person to write an up-to-date textbook on this subject.

Various methods can be followed to prepare such a textbook. Each chapter can be written by a different author and an editor can try to unify the different texts. Usually the result of such an inhomogeneous collection of papers is unsatisfactory.

It was felt that a more homogeneous book could be obtained if one author prepared the table of contents and were responsible for the writing of the whole book, assisted in various specialized sections by experts in different fields of biometeorology.

With 8 exceptions, all collaborators of this book are members of the International Society of Biometeorology. Both in the table of contents and at the beginning of each specialized section the name of the contributor is clearly indicated.

The present book is written for post-graduate medical students, physicians, veterinarians, biologists, meteorologists and other branches of science related to biometeorology. It has not been our aim to write a complete textbook. Our main purpose is to review this whole field, to indicate the principal facts known so far and the many problems which remain to be solved. At the end of the book there is a very extensive bibliography, classified in different groups of references belonging to each section discussed. This will enable the reader who wants to continue biometeorological research in a particular field to do so without extensive reference research. Owing to this system, several references have been mentioned more than once, as we were anxious to make each reference section as complete as possible.

The book is intended to be an *introduction to medical biometeorology*. The medical reader may be wondering why this book was written by a meteorologically and physiologically trained geophysicist and field geologist and not by a physician. The reason is the following. Biometeorology is a new, independent science, a border-science which belongs neither to meteorology nor to medicine. It is a field of science in which the geophysicist or meteorologist and the physician meet and work together rather than try to compete. It requires a special training from both and it is immaterial whether the subject is studied by a meteorologically trained physician or by a physiologically trained geophysicist or meteorologist.

In the 20th century many books have been written on biometeorology[1-21]. Those of two authors deserve special mention.

Between 1934 and 1938 William F. Petersen (Professor of Internal Medicine and Head of the Dept. of Pathology and Bacteriology at the University of Illinois, College of Medicine at Chicago, U.S.A.) wrote a number of voluminous monographs on *The Patient and the Weather*, which studies were followed in 1947 by a summary *Man, Weather, Sun.* These monographs dealt with meteorological influences on the normal person and on the patient. Petersen described his book as "a book of pictures and maps dealing with the human beings that populate the land maps that show why they are what they are and why they are becoming more so; why some become able and others dull; why some states are radical, while others are fundamentalist, why Vermont produced more genius but also more insanity, why individuals die of tabes and paresis in a clear-cut track right across the country, while to the North and to the South the death rate falls; why the Negro lives to a ripe old age in South Carolina but becomes an 'autonomic problem' in the North".

On the European side of the Atlantic Ocean another scientist in the field of biometeorology should be mentioned, Professor B. De Rudder, Director of the Dept. of Pediatrics at the University of Frankfurt. In his 300-page book *Grundriss einer Meteorobiologie des Menschen. Wetter und Jahreszeiteneinflüsse,* of which 3 editions have already appeared (in 1931, 1938 and 1952), an excellent summary was given of various aspects of biometeorology. His critical analysis of the vast amount of literature in the field of biometeorology was refreshing and helped considerably to overcome many misconceptions of his medical colleagues.

After what has been said in the previous paragraphs it may seem superfluous for a new textbook on biometeorology to be written so soon after the publication of the standard works of Petersen and De Rudder. It was for this reason that the present author was very reluctant to undertake the preparation of this volume. However, several considerations persuaded him to do so.

Biometeorology had developed rapidly in the last 5 or 10 years, chiefly as a result of many environmental physiological studies carried out more particularly in Great Britain and the U.S.A. The previous textbooks on biometeorology gave summaries of a wealth of observations, but, for various understandable reasons, the deeper physiological mechanisms involved were dealt with superficially. The creation of the International Society of Biometeorology in 1956 made it possible to obtain a better world view of the various aspects of biometeorology studied in the past and at present. For the reasons given, the preparation of a small modern textbook on biometeorology would seem to be warranted.

After introductory Parts on the classification and definition of various branches of biometeorology and the principal biometeorological concepts, a review is given in Part II of the principal meteorological factors, physical, chemical and physico-chemical, which should be recorded in biometeorological research.

This part, too, reviews the significance of various air-polluting substances—partly the result of rapidly increasing industrialization in the Western countries—and briefly discusses means of prevention.

Finall, recent studies of the possible effect of extraterrestrial factors on the living organism will be discussed very briefly. After a description of the biometeorological methods used (Part III), Part IV deals *in extenso* with the effect of weather and climate both on healthy man and on diseases. Most points of interest are only briefly reviewed but an extensive list of references at the end of the book enables the reader to study the problem in more detail if he so wishes.

Various modern methods of biometeorological treatment are considered as well as the observed weather-disease relationships and the possible physiological mechanisms involved, because most clinicians are not acquainted with this new approach to medical treatment. The effect of town planning and architectural design on the health of man—a very important and often neglected medical problem—receives attention at the end of Part IV.

Part V deals with the influence of weather and climate on the animate world surrounding man. This being a very vast field, only those aspects are reviewed which are of direct importance to man; but the effect of insects is discussed more extensively in view of the part they play in the origin and distribution of various diseases.

On account of the significance of biometeorology to future space travel, a special part (Part VI) is devoted to the problem involved in the control of microclimates in space-craft.

The book concludes with a chapter on graduate training in human biometeorology, a subject, which has hitherto been sadly neglected in most medical schools of the world.

As mentioned before, it would have been impossible for one author to cover, unaided, each of the subjects mentioned above. It was only by the close cooperation of a large number of biometeorological experts in different parts of the world that the material for the book could be collected. The names of these scientists, their specialties and present function are summarized in the list of contributors given at the beginning. It is fully realized that many aspects have hardly been touched on, but, if the present publication helps to bring biometeorology more into the foreground of modern science, we shall all feel gratified and rewarded for the labour involved in the compilation of the data required.

DEFINITION AND CLASSIFICATION OF BIOMETEOROLOGY

In our introductory remarks biometeorology was rather briefly defined as the science studying the influence of *weather* and *climate* on the living organism. The two concepts "weather" and "climate" are often not clearly distinguished by the non-meteorologist.

The *climate* of a region represents the average weather condition of that region, in other words the average of the total group of phenomena in the atmosphere above the region, such as temperature, humidity, wind speed, etc., characterized by certain figures, which represent the average values observed during a period of 30 years.

Weather comprises the group of day-to-day changing meteorological conditions such as temperature, rainfall, snow, etc.

In 1956 *biometeorology* (the study of the influence of weather and climate) was more scientifically defined by the members of the International Society of Biometeorology during a Biometeorological Symposium held at Unesco Headquarters in Paris from 29–31 September 1956. Their definition reads as follows:

"Biometeorology comprises the study of the direct and indirect interrelations between the geophysical and geochemical environment of the atmosphere and living organisms, plants, animals and man.

The term 'environment' is broadly conceived and includes micro, macro and cosmic environments in so far as they affect the earth's atmosphere and the diverse physical and chemical factors which comprise these environments. The investigations in these disciplines should be conducted in nature or in the laboratory under as rigidly controlled conditions as possible to describe measurable and reproducible physical, chemical and biological factors which show a sufficiently high statistical correlation with measurable physiological and pathological processes to suggest a valid cause and effect relationship between organism and environment."

As biometeorology comprises the study of the influence of weather and climate on *plants, animals* and *man,* the biometeorological sciences have been divided into the following five main groups: phytological, zoological, human, cosmic and paleo-biometeorology.

(1) *Phytological biometeorology* studies the influence of weather and climate on the development and distribution of plants for general phytological, agricultural and forestry purposes, but also the effects on small plant organisms responsible for the development of plant, animal and human diseases.

(2) *Zoological biometeorology* studies the influence of weather and climate on animals in general, milk production of cows, etc., but in particular the effect of weather and climate on insects and terrestrial arthropoda, their physiological activities and development and the outbreak of plant, animal and human diseases caused by these insects. We may refer to the studies on locust swarms, malaria mosquitoes, etc.

(3) *Human biometeorology* studies the influence of weather and climate on man. It is usually divided into four important sections: (*i*) *Physiological biometeorology* (the influence of weather and climate on physiological processes in normal healthy man); (*ii*) *Social biometeorology* (use of favourable meteorological factors for the treatment of large population groups as preventive or curative measures); (*iii*) *Pathological biometeorology* (influence of climate and weather on the various physiological and pathological phenomena associated with the diseases of man, the period of outbreak, intensity and geographical distribution) and (*iv*) *Urban biometeorology* (the influence of the microclimates in houses and cities on the health of man, the effect of architectural constructions and town planning on these microclimates).

Of special importance for the general practitioner are the results obtained in *acclimatization biometeorology* (a branch of physiological biometeorology which studies the various physiological processes involved during adaptation to extreme conditions of temperature, humidity etc., *e.g.* in the tropics); *air pollution pathology* (influence of pollen, dust and chemical air pollution on man) and the various methods applied in *climatotherapy.*

(4) *Cosmic biometeorology* studies the influence of extraterrestrial influences such as variations in solar activity, cosmic radiation, etc. on living organisms.

(5) *Paleo-biometeorology* studies the influence of climatic conditions in the past (millions of years ago) on the development, evolution and geographic distribution of plants and animals on earth.

According to the methods of research which have been applied, biometeorology has also been subdivided into *empirical* and *experimental biometeorology*.

Empirical biometeorology (from the Greek word empeiria = experience) collects observations of biometeorological facts or events and the knowledge resulting from them without a preconceived idea or theory, whereas in the case of *experimental biometeorology* (from the Latin word experiri = to try) observations of facts or events are collected during a trial set-up with the purpose of testing a special hypothesis, theory or assumption.

(1) In *empirical biometeorological studies* certain physiological or pathological phenomena in man, animals or plants, caused or triggered by atmospheric agents, are collected on a statistical basis but in general without any preconceived idea. Usually there are no clear-cut, quantitative relations between the atmospheric agent and the observed biological effect.

Two types of studies can be distinguished in empirical biometeorology: In the first group the effect of more or less known atmospheric agents are being studied. They are either specific meteorological factors (temperature, humidity, etc.) or groups of such factors. In these studies the effects observed are often basically reproducible. However, in the second group the effects are studied of either little-known or unsuspected atmospheric agents on certain biological phenomena, the results being based on statistical data and often difficult to reproduce.

(2) In *experimental biometeorology* observations are collected on exactly measurable changes in man, animals or plants under reproducible, sharply controlled experimental conditions, both in the laboratory and in the field. The different conditions are the result of measurable environmental factors, the effect of which is generally understandable from the physical, chemical and (or) biological point of view and usually enables us to predict the qualitative and quantitative aspects of responses to those particular environmental conditions. As stated above, the purpose of these observations is usually to test a special theory, hypothesis or assumption.

Although the workers in both fields of biometeorology are often inclined to consider their approach as the most scientific and promising one, it should be realized that the two methods are actually complementary. It is only due to empirical biometeorology that a vast number of weather–disease relationships were discovered. However, the explanation and medical application of these observed relationships has only been possible due to the studies of experimental biometeorology.

In order to understand the wide scope of biometeorology, a detailed classification of the five principal groups, as described above, is given below. The classification and definitions of each section are based on the most recent classification used by the International Journal of Biometeorology, which has been published by the International Society of Biometeorology since July 1957.

I. PHYTOLOGICAL BIOMETEOROLOGY

Sect. A. General phytological biometeorology
Sect. B. Agricultural biometeorology
1. General agricultural biometeorology
2. Agricultural phenology
Sect. C. Forest biometeorology
Sect. D. Physiological phyto-biometeorology
Sect. E. Pathological phyto-biometeorology

II. ZOOLOGICAL BIOMETEOROLOGY

Sect. A. General zöological biometeorology
Sect. B. Physiological zoo-biometeorology
Sect. C. Entomological biometereology
Sect. D. Veterinary biometeorology
Sect. E. Pathological zoo-biometeorology

III. HUMAN BIOMETEOROLOGY

Sect. A. Physiological biometeorology
1. General physiological biometeorology
2. Geographical biometeorology
3. Ethnological biometeorology
4. Acclimatization biometeorology
Sect. B. Social biometeorology
1. General social biometeorology
2. Psychological biometeorology (including aestheto-biometeorology)
3. Archeological biometeorology
Sect. C. Pathological biometeorology
1. General pathological biometeorology
2. Meteorological pathology
3. Climatological pathology
4. Air pollution biometeorology
a. Pollution with organic particles (pollen, fungi, etc.)
b. Pollution with inorganic particles (dust, etc.)
c. Chemical pollution
d. Aerosol biometeorology

5. Geographical climatopathology
6. Climatotherapy
   a. General climatotherapy
   b. Thalassotherapy (climatological-)
   c. Heliotherapy
   d. Thermotherapy
   e. Aerosol (and inonization) therapy
   f. Socio-climatotherapy
   g. Climatic health resorts
   h. Climatic chamber treatments

Sect. D. Urban biometeorology
1. General urban biometeorology
2. Architectural biometeorology
3. Sanatorium biometeorology

Sect. E. Nautical biometeorology
1. General nautical biometeorology
2. Cargo biometeorology

IV. COSMIC BIOMETEOROLOGY

Sect. A. General cosmic biometeorology
Sect. B. Special cosmic biometeorology

V. PALEO-BIOMETEOROLOGY

Sect. A. Phyto-paleo-biometeorology
Sect. b. Zoo-paleo-biometeorology
Sect. c. Paleo-climatopathology

Most of the titles of the classification given above are self-explanatory. However, a number of them require a more specific definition.

Entomological biometeorology: Study of the influence of weather, climate and cosmic factors on insects and other terrestrial Arthropoda.

Veterinary biometeorology: Study of the influence of weather, climate and cosmic factors on domestic and farm animals and birds and on animal products such as eggs, wool, milk, etc.

Geographical biometeorology: Study of the influence of geographical differences on the physiological processes of normal, healthy man. This branch of biometerorology is actually a part of medical geography.

Ethnological biometeorology: Study of the influence of weather and climate on race and body structure of man.

Acclimatization biometeorology: Study of the adaptation of the human body to extreme climatological conditions (due to temperature changes, high altitude, etc.).

Social biometeorology: Study of the influence of weather and climate on the social habits of man.

Psychological biometeorology: Study of the influence of weather and climate on the mental processes of man.

Aestheto-biometeorology: Study of the influence of weather and climate on the aesthetic expression of man (architecture, painting, music, etc.).

Archeological biometeorology: Study of the influence of weather and climate on the origin, distribution and disappearance of past civilizations.

Meteorological pathology: Study of the influence of specific single meteorological components (temperature, humidity, etc.) or groups of components on the origin and frequency of diseases and on the physiological phenomena of the diseases of man.

Climatological pathology: Study of the influence of different climates (marine, forest, mountain, etc.) and their seasonal variations on the origin and frequency of diseases and on the physiological phenomena of the diseases of man.

Air pollution biometeorology: Study of the pathological influences of air pollution (either organic or inorganic particles or chemical substances) on man.

Aerosol biometeorology: Study of the biological effects of aerosols (*i.e.* gaseous, liquid or solid aggregates floating in the air, with diameters of 1/1000 to 10 μ and consisting of hundreds to millions of molecules, often with either positive or negative electrical charges).

Geographical climatopathology: Study of the geographical distribution of diseases as a result of geographical differences in climate and in single or in groups of meteorological factors.

Climatotherapy: Study of the therapeutic influence of certain climates and meteorological conditions on the diseases of man.

Thalassotherapy (climatological-): Study of the therapeutic influence of marine climates on man.

Heliotherapy: Study of the therapeutic influence of solar radiation on man.

Thermotherapy: Study of the therapeutic influence of various forms of heat on man.

Aerosol therapy: Study of the therapeutic influence of certain aerosols on man.

Socio-climatotherapy: Study of construction methods of schools, of location and construction of holiday camps for children and of other social aspects of life as a function of climate and weather and of the methods for improvement of the favourable climatological effects.

Climatic chamber treatments: Application of sharply controlled microclimates produced in specially constructed climatic chambers, as treatment of various diseases.

Sanatorium biometeorology: Study of the best location and construction methods of sanatoria from the point of view of climate and weather.

Nautical biometeorology: Study of the physiological and pathological phenomena observed by ships' surgeons (both naval and mercantile marine), in man and animals in various climates at sea.

Cargo biometeorology: Study of the influence of climate at sea on the living cargo in ships (plants, fruits and animals).

PART I

Principal Biometeorological Concepts

In a previous section two important meteorological concepts were defined, the difference between *climate* and *weather*, climate representing the average long-term weather conditions in an area, whereas weather is a short-term concept. However, apart from these two important meteorological concepts, there are several more, which will be briefly discussed in order to facilitate the reading of the following chapters. Those who would like to do personal research in the field of biometeorology should study these concepts in greater detail in the various meteorological textbooks[39-62].

In recent years a sharp distinction has been made between *macro-* and *micro-climate;* the first term comprises the climatic conditions of the total atmosphere above cities, provinces or countries, whereas micro-climate refers to the air directly surrounding the living organism in a room, factory or in mines. The differences in physical and chemical properties are usually considerable and serious mistakes are often made if a certain "meteorotropism" is correlated with the macro-climate only. Micro-climate is a function of macro-climate but it has its own specific properties. How much the micro-climate depends on the macro-climate will be discussed later in Part II, Chapter 1, p.82.

Around 1919, an important biometeorological concept was introduced by the Norwegian meteorologists V. and J. Bjerknes, the concept of *air mass,* a term used to denote large masses of air in the atmosphere with roughly the same physical and chemical properties (temperature, humidity, etc.), extending in a horizontal direction over hundreds or even thousands of kilometres and in a vertical sense over more than one kilometre. Depending on the *source area* of the air mass meteorologists distinguish between polar, arctic, continental, maritime, tropical air masses, etc., briefly indicated as Pm (Polar maritime), Tm (Tropical maritime), etc. One of the first general classifications was proposed in 1928 by T. Bergeron. The air masses usually differ in electrical properties (*e.g.* ionization), temperature, humidity, etc. but also in chemical properties such as ozone content, acidity, etc. (Fig. 1).

If two air masses meet, *e.g.* polar and tropical air, as often happens on the Atlantic Ocean, they often do not mix and remain separated by a boundary flane, which is a surface of discontinuity known as *frontal surface.* The line of intersection of a frontal surface with the surface of the earth is called *front line* or just *front.* The frontal surface is usually inclined. The cold heavy air tries to move under the lighter warm air mass. If warm air moves towards an area with cold air, we speak of a *warm front* (slope of 1:100 up to 1:400); if cold air moves towards a warm area, it is called *cold front* (slope 1:30 to 1:100).

The contrast in temperature and, therefore, in density affects the pressure

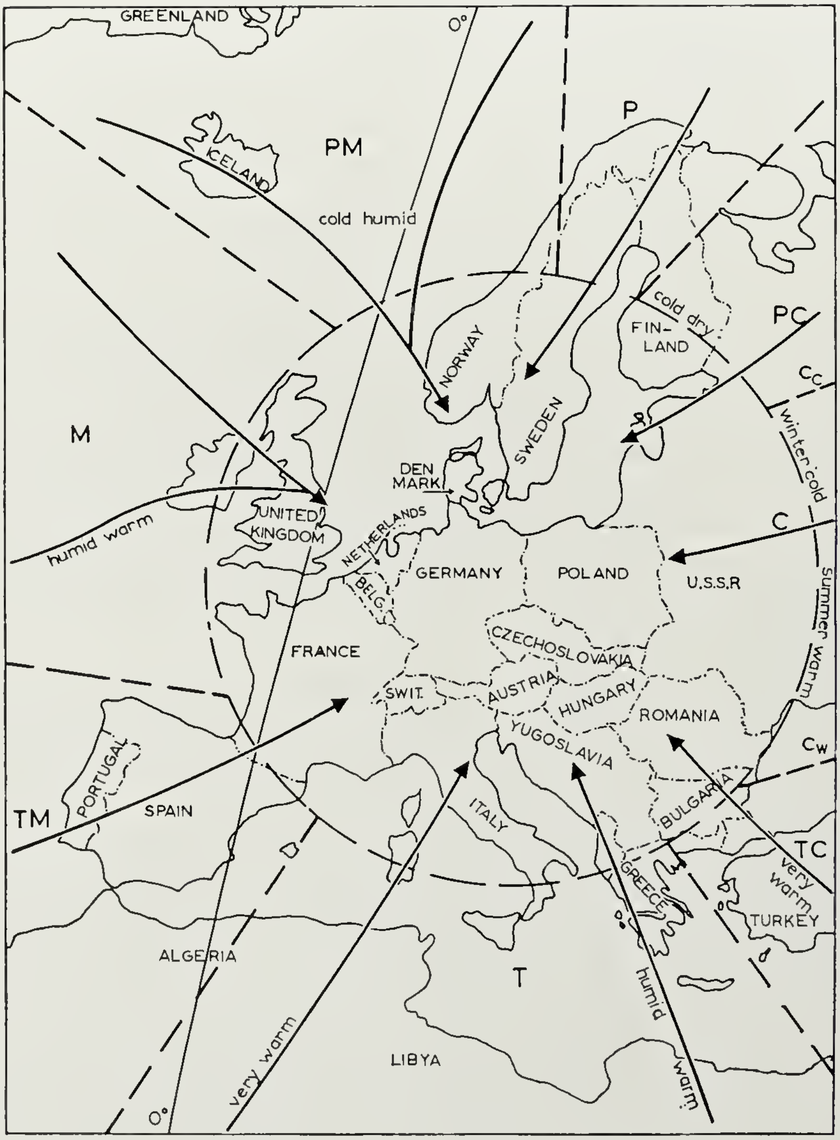

Fig. 1.
Air masses in W. Europe, their average temperature and humidity (based on map of Linke).

and wind distribution. The lines of equal atmospheric pressure (*isobars*) show a sudden bend at the front line and, as a result, the direction of wind, pressure gradient (gradient being the change of a meteorological element per unit of distance) and wind velocity may change abruptly on both sides of a front. The fronts often lie along a trough of low pressure and are usually accompanied by rainfall. Rainfall usually occurs when a sharp discontinuity between the air masses exists which is characterized by steep temperature and pressure gradients which extend upwards in the atmosphere over 1000 metres and more.

If a cold front overtakes a warm front, the whole warm front is pushed upwards. The warm air is closed off from the earth's surface, a phenomenon known as *occlusion.*

Usually the temperature falls in the atmosphere with increasing height. However, sometimes at a certain level a temperature increase occurs, known as *inversion of the temperature gradient* (or briefly known as *inversion*), another important biometeorological concept. Inversion indicates thermal stability of the atmosphere and absence of "*turbulence*" (*i.e.* irregular or "eddy" motion of the air particles or air currents). It occurs, for example, at the top of a fog layer or at the top of certain clouds of the so-called *stratus type* (*i.e.* uniform layers of clouds resembling fog, but not resting on the ground).

Inversions are common in temperate climates at night between the ground and about 100 metres high, where the sky has been clear for several hours and the wind has not been very strong. In W. Europe during *anticyclonic* weather (*i.e.* periods with high atmospheric pressure) in winter, this surface inversion may grow until it extends to a considerable height and it may then persist for several days. The dense fogs which characterize some cities, like London in winter, usually originate from such an inversion. Accumulation of smoke overhead may produce complete darkness at midday in a city if the inversion is sufficient to prevent the smoke from dispersing. This process can become very serious and may cause the notorious *smog* (smoke-fog), a very dense fog polluted with soot particles and other volatile chemical substances (see p. 142).

In December 1930 about 60 people died at Huy (in the valley of the river Meuse in Belgium) because of heavy smog lasting several days, caused by an inversion layer being 70–80 metres above the heavily industrialized valley. The fog was polluted with sulphuric acid, sulphur dioxide and fluor gases. On 30 October 1948 about 20 people died at Donora (Pennsylvania) in the U.S.A., and 70% of the population over 50 suffered from serious lung trouble. Again sulphuric acid was the cause of the disaster. In July 1953 roughly 400 people died in London as a result of smog. The problems of air pollution and smog will be discussed in fuller detail by P. J. Meade on page 142.

We have just mentioned the concept of an *anticyclonic* or *high pressure area* (H.P.A.) in contrast to a *depression, cyclonic* or *low pressure area* (L.P.A.), characterized by low barometric pressures surrounded by relatively higher pressures.

The characteristics of a L.P.A. depend on the temperature distribution. If the temperature is lowest at the centre, the L.P.A. will increase in intensity aloft. If the temperature is highest at the centre, the L.P.A. will decrease aloft; therefore depressions are classified into *cold-core* and *warm-core* L.P.A.'s Influx of cold air in a L.P.A. will intensify its activity, warm air will weaken it.

The general world-wide distribution of these pressure areas differs during summer and winter and is different for the northern hemisphere, with its large land area and more marked contrast between summer and winter conditions, from what it is for the southern hemisphere with its predominating ocean area. The most important characteristics of the pressure distribution are the following:

(1) Just south of the equator, a belt of L.P.A. occurs in January especially over the warm continents of the southern hemisphere. In July this equatorial L.P. belt lies north of the equator over the warm land masses of the northern hemisphere.

(2) In the sub-tropics of the southern hemisphere (about 30–40° southern latitude known as the *horse latitudes*) a belt of H.P.A. occurs with centres over the Pacific, Atlantic and Indian Ocean. In the northern hemisphere, north of the 30° latitude, H.P.A.'s are found (particularly in July), in the Pacific (west of the U.S.A.) and in the Atlantic Ocean, in winter also in Central Asia.

(3) In winter deep L.P.A.'s occur in the North Pacific and N. Atlantic Oceans.

The origin of the L.P.A. and H.P.A. are mainly determined by differences in temperature. A depression usually originates on a stationary frontal surface, where the wind on the two sides is blowing parallel to the front, with strong shearing motion. As a result of a slight decrease in pressure along the front, for example due to local heating (causing a vertically rising air current and inflow along the surface), or due to pressure changes at higher levels in the atmosphere, the originally straight frontal surface becomes bent and as a result of pressure differences the air particles begin to move, causing the so-called initial *cyclonic vorticity*.

Owing to the *Coriolis force,* which is the result of the rotation of the earth, in the northern hemisphere the air currents are moved to the right (if we face the direction of air movement, our back against the wind), in the southern hemisphere to the left. Consequently, in the northern hemisphere the L.P.A. always lies to the left of the direction of air movement (law of Buys Ballot). The acceleration of the Coriolis force (a) depends on the speed of air movement (v), rotational speed of the earth (ω) and latitude (φ):

$$a = 2 v \omega \sin \varphi$$

As a result of this mechanism, the air currents moving towards the point of lowest pressure along the front are deflected and the initial *cyclonic vorticity* is strengthened.

In view of the fact that the Coriolis force is rather small, cyclonic vorticity develops only if the air moves far enough (*i.e.* a few miles) for the Coriolis force to act. If air currents move towards a centre without vorticity, a chimney-like rise of air occurs. This takes place near the equator, where the Coriolis force approaches zero, or with small circulations of air, only a few miles across, causing small *tornado funnels* with intense rotary movements around a local low pressure centre. As stated before, the basic cause of air movements is the difference in temperature between two areas. Over land in hot areas, the air is heated and rises because of decreased density. Cool, heavier air from the ocean (or a large lake) may flow in to take its place. If this happens on a continental scale, as in India, it is called a *monsoon* circulation. Conditions may be reversed because the ocean water may retain its warmth for a longer period and the land cools off more quickly. Instead of a *sea breeze,* a *land breeze* towards the sea may develop. In certain countries it is a diurnal phenomenon, a sea breeze during the day and land breeze late at night. A similar phenomenon in mountain areas causes a *valley breeze* when, during the day, cool air in a valley moves into the warmer areas of the surrounding mountains. At night the mountains cool off more quickly and a *mountain breeze* develops towards the valley, which thermal process is aided by the gravity forces.

Apart from monsoons, the tropical regions between 30°N and 30°S are characterized by so-called *trade winds,* because air from both hemispheres streams toward the equator. Due to the Coriolis force, these winds blow north-east in the northern hemisphere and south-east in the southern hemisphere. As a result of these opposing steady winds, near the equator a zone occurs known as the *doldrum belt,* characterized by light winds, low pressure and strong vertical convection and wide-spread shower activity. It is north of the 30° latitudes that the above-mentioned horse latitudes begin with the subtropical high pressure belt. At low latitude the prevailing wind direction in this belt is easterly, in higher latitudes westerly.

West winds prevail north and south of the horse latitudes to about 55° latitude. This belt is known as *zone of prevailing westerlies.* It is the region of great cyclonic storms and temperature contrasts which, in the northern hemisphere, affect the life of W. Europe, Canada and the northern parts of the U.S.A. In the southern hemisphere it is known as the *roaring forties,* with its strong, steady west winds. It is in these areas north of the horse latitudes that warm tropical and cold polar air masses meet. North of 65° latitude the winds swing around again and become mainly easterly.

For reasons of convenience, the atmosphere is divided into a number of layers. The lowermost part is called the *troposhere,* the zone where all the storms, clouds and important weather changes occur. Temperature decreases upwards (*ca.* 6.5°C/km or 3.6°F/1000 ft.) and reaches a minimum at the top, known as the *tropopause.* The greatest height, which is above the equator, amounts to 15–18 km with a temperature at the tropopause of —85°C (—121°F). Over the poles at an elevation of 7–10 km it is —60°C (—76°F).

At the tropopause a sharp temperature inversion occurs. Above it the temperature of the air increases upward. At the upper levels in the troposphere (about 600–900 m below the tropopause) narrow belts of high-speed winds occur known as *jet streams,* having sharp boundaries with the relatively stagnant surrounding air masses. The velocity fluctuates between 240 and 640 km/h. This may cause great turbulence near these jet streams. It has been assumed by a group of meteorologists that deflection of these eastward-flowing jet streams, due to the Coriolis force, may cause a piling up of air to the south of the zone of prevailing westerlies which may contribute to the formation of the high pressure belt of the horse latitudes.

Above the troposphere lies a region known as *stratosphere,* marked by almost complete lack of clouds and slight turbulence. It is divided into three layers: a lower cold *isothermic layer* 12–35 km above sea level with fairly constant temperatures (around —50°C), followed by a *warm layer* (up to 60 km above sea level) with sharply rising temperatures over 50°C (ca. 5°C/km) and a very cold *upper layer* (up to 80 km above sea level) with temperatures of —70°C. The warm layer lies near the top of a region in the atmosphere with maximum ozone concentration (see p. 87) and maximum absorption of ultraviolet radiation. Some meteorologists believe that ozone plays an important role in stratospheric circulation and therefore may considerably influence the general weather conditions in the world*.

On top of the stratosphere lies the *ionosphere* (60–80 km above sea level) characterized by strongly ionized air causing the reflection of radio waves (Heaviside layer) and the various auroras (northern lights) in the atmosphere. The lowest reflecting layer, known as *D-layer* ranges from 60–100 km. It

* Recent studies by MacDonald and Roberts at the High Altitude Observatory of Colorado suggest that L.P.A.'s at an elevation of 10,000 m in the atmosphere may change suddenly in shape a few days after heavy solar eruptions.

reflects low-frequency radio waves but absorbs medium and high-frequency waves. The layer disappears as soon as the sun sets and during periods of pronounced sun flares. The ionization of the layer may be caused by dissociation of oxygen or ozone molecules due to intense ultraviolet radiation as a result of eruptions in the sun's chromosphere. However, this question is still unsettled.

Between 90 and 130 km a so-called *E-layer* occurs, which strongly reflects medium- and high-frequency radio waves. This ionizing layer is usually explained as being produced by ultraviolet photons from the sun acting on oxygen and nitrogen molecules. The layer becomes thinner during the night.

Above the E-layer various other layers are distinguished: the *E_2-region* (at about 150 km height), the F_1- and *F_2-region*, the *G-region* (around 400 km). It is at a height of between 80 and 300 km that the northern lights are usually formed as a result of the bombardment of oxygen and nitrogen molecules by electron and proton showers from the sun.

Above the ionosphere the density of the atmosphere becomes very low. This outermost sphere is often named *exosphere* after L. Spitzer. It is largely thanks to the observations during the recent Geophysical Year and the outer-space research of the U.S.A. and U.S.S.R. that our knowledge has increased enormously.

For example, satellites used for high-altitude cosmic ray research have demonstrated the existence of a zone with very intensive radiation known as *Van Allen radiation*, after the first investigator J. A. Van Allen of the University of Iowa, U.S.A. The radiation seems to be due to protons and electrons concentrated in several belts around the earth. The lowest belt reaches a maximum intensity at about 2400 km altitude; the upper belt has a zone of maximum radiation at 32,000 km up. There is evidence for a third and lower belt with an extremely intense radiation fatal to human beings if exposed to it for more than one hour. It seems to be caused by direct emission from the sun and by the decay of cosmic ray neutrons created within the earth's atmosphere that are directed outward.

Sudden decreases in intensity have been observed, known as *Forbush decreases* which show a latitude dependence. The decreases are largest near the poles and reach a minimum near the magnetic equator. They are closely related to sudden geomagnetic changes created by sun flares. From the point of view of bioclimatological research, in all probability the various phenomena are determined by the troposphere only. However, studies by Piccardi[413–420] and others seem to suggest that the influence of other spheres in the atmosphere is not negligible (see pp. 149–153).

Another important concept in biometeorology is that of *weather phases* which was introduced by the German meteorologist H. Ungeheuer[59-61], formerly head of the medico-meteorological research station at Bad Tölz, Bavaria (Germany). After reading the following chapters the reader will be aware that as a rule no single meteorological factor is responsible for observed weather-disease relationship, but rather a complex group of factors. Because of the intricacy of the problem and in view of the difficulty of distinguishing between the individual meteorological components responsible for the biological effect, Ungeheuer has classified the complex daily weather changes in Bavaria into six phases, to which he has given the following names: average nice weather; very nice weather; extremely nice weather with slight foehn condition; initial weather change; complete weather change; initial weather improvement. These weather phases in Bavaria are accompanied by the following meteorological characteristics:

Phase 1. *Average nice weather:* Partly cloudy sky (varying in degree of cloudiness) with the usual daily variations in temperature and humidity. Barometric pressure is rather high. The weather has a "cool dry refreshing effect" on the human body.

Phase 2. *Very nice weather:* Decreasing cloudiness, slight fall in barometric pressure, pronounced rhythmic changes of the temperature-humidity curves. The weather is experienced as "pleasantly warm".

Phase 3. *Extremely nice weather with slight foehn* condition:* Few lenticular clouds and first cirrus clouds; barometric pressure is already falling considerably; temperature is rising as a result of the increased effect of solar radiation and the influx of warm dry air. The weather is usually experienced as "unpleasantly warmish or warm" (muggy).

Phase 4. *Initial weather change:* Rapid increase of rain and thunderstorm clouds; continued steep fall in barometric pressure; temperature remains high but humidity increasing. The weather is experienced as "sultry and oppressive".

Phase 5. *Complete weather change:* Sudden influx of cold air under a heavily clouded sky accompanied by a cold front and rain showers; after the passage of the front, barometric pressure rises, temperature falls steeply, humi-

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* *Foehn* (from the Latin word Favonius = warm South to South-Westwind) is a common name in Switzerland used for a very warm and very dry wind which often blows in the mountain valleys of Switzerland and Tyrol. It originates if humid air from Italy rises against the high mountains of the Swiss Alps. This impact cools it so much that heavy precipitation results. The dried air which reaches the Northern lower parts of the Alps warms up during this process and blows as a warm dry wind in the Northern valleys. A similar wind is known in the Western plains of the U.S.A. as *Chinook*, as *Santa Ana* in S. California, as *Zonda* in the Argentine, as *Koebang* and *Gending* in Java, as *Bohorok* in N. Sumatra, as *Autan* in Central France or *Tramontana* in N. Italy. They are characterized by peculiar biological effects which also show up in the expression "losing one's tramontana" (to be put out).

dity is rather high. The weather is experienced as "uncomfortable penetrating cold".

Phase 6. *Initial weather improvement:* Sky becomes less cloudy, blue patches appear; temperature is still low but during the day the temperature rises; humidity falling. The weather is experienced as "pleasantly stimulating, cold".

It is evident that this particular classification applies only to a restricted area like Southern Bavaria, but similar single classifications could be worked out for any area in the world.

About 70 patients in Bad Tölz daily reported their various subjective complaints, which were correlated with these weather phases. Obviously, objective physiological check-ups should be made to verify the accuracy of such reports, lest patients, eager to interpret their symptoms in the light of "the weather", mislead the physician.

An analysis of daily blood pressure and pulse changes of 20 healthy people aged 20 for 150 days (observed at the Surgical Clinic of the University of Munich), before and after a load experiment, indicated (according to Ungeheuer) that during weather phases 1 and 2 blood pressure and pulse frequency increased compared with the average values; during phases 3 and 4 they decreased and during phase 6 they became normal again.

Similar studies at Munich concerning pain sensitivity and capillary resistance (see later p. 335) showed that in phase 2 capillary resistance increased, pain sensitivity decreased, in phases 3, 4 and 5 the reverse was observed, while during phase 6 conditions became normal again.

An analysis of the daily number of accidents in a large machine factory at Munich (with 3000 labourers) during 1955 showed an increase of 50% in the number of accidents during days within phases 3, 4 and 5 (about 18–19 minor accidents a day), as compared with phases 1, 2 and 6 (about 12 a day). Although these problems will be discussed more fully in Part IV, Chapter 2 (p. 675), we have here given these examples to demonstrate the usefulness of "weather-phase analysis" as an initial empirical approach before a more detailed meteorological and experimental approach may help us to understand the deeper physiological mechanisms involved.

Apart from the concept "weather phases", the biometeorologist often uses the expressions *sea, land and mountain climate.*

In sea-water the sun's rays penetrate more deeply than in soil and as particles of water move around, the heat is better distributed. Furthermore, water has a greater specific heat than minerals or rocks (1 against 0.2). Due to these three factors the sea warms up more slowly than the land with the same amount of solar radiation. On the other hand, water will cool more slowly than the land. Consequently climate above the sea differs considerably from that above land and it is therefore reasonable to distinguish between land and sea climate.

A typical *sea climate* is often defined as the climate of an area near the sea where the difference in average temperature of summer and winter is less than 15°C; a typical land climate has differences of more than 20°C. However, the same temperature conditions of a sea climate, are also found in most equatorial regions.

In N.W. Europe the boundary between land and sea climate may start very close to the North Sea. Characteristic differences are given in Table 1.

TABLE 1

Along the coast	*Inland*
1. Centres of depressions, active fronts and strong winds may occur in the coastal area only. General turbulence is usually greater.	1. Fronts often quickly lose their activity inland. Average wind velocity is lower; less stormy weather.
2. Winter temperature is relatively high, with few frosty days; summer temperature is rather low	2. Cold winters with many days of frost and warm summers.
3. Highest precipitation in winter, fewer days of rain and snow; hail is common in autumn and winter.	3. Highest precipitation in summer more days of rain and snow during the year; hail is common in spring.
4. Thunderstorms are often related to centres of moving depressions along the coast; the duration may be prolonged.	4. In summer many thunderstorms occur due to extreme heat, but are usually of short duration.
5. The number of hours of sunshine is often higher than inland (1650 h/year in the Netherlands).	5. Number of hours of sunshine only 1500 in the Netherlands.

At great elevation on land, both the amounts of heat radiation received during the day and lost during the night are entirely different from lowland conditions. The average daily temperature in mountains is usually lower; there is usually less general turbulence of the atmosphere; the ultraviolet radiation is often 30% stronger and smaller wavelengths reach the surface which are absorbed by the atmosphere in low-lying land; there is usually less water vapour and, as a result, the heat loss from the earth is therefore greater than at lower altitudes; the general atmospheric pressure and the partial pressure of oxygen (see p. 293) is lower; often the ozone content is higher; electric conditions of the atmosphere are mostly different (*e.g.* the number of large ions per cm^3 drop from 10^4 at low altitude, to 10^2 in the

Alps; however, the small ions increase in number). As further explained on p. 298, these various differences in meteorological conditions have different biological effects, which shows why "mountain climate" is a useful biometeorological concept. Mountains have also an important indirect biometeorological effect. Monsoon winds may be either dry or wet if they meet a mountain, range or volcano. The lack of high mountains in W. Europe makes it easy for west winds to penetrate deeply into the centre of Europe, in contrast to Scandinavia, where the sea climate is restricted to a small strip along the Norwegian coast. The latter is true for the west winds in South and North America. On the other hand, in the U.S.A. the lack of east-west mountain ranges enables cold polar air form Northern Canada to reach the Southern States in a few days, and warm tropical air off the Caribbean Sea may reach Canada. These very rapid weather changes may cause important biometeorological effects both in the U.S.A. and in W. Europe.

Apart from the three climatic types just described, various classifications have been proposed of which the classification of Köppen is best known, despite its shortcomings. This classification, like may others, is based only on temperature and precipitation. As we shall see later on, many other factors are important from a biometeorological point of view. Köppen's classification is as follows:

(1) *Hot rainy climates*

(*a*) *Tropical rain forest climate:* Hot humid climates of the doldrums; mean temperature of coldest month over 18°C, annual temperature range less than 3°C; heavy rainfall (at least 6 cm in driest month); luxuriant vegetation with dense forests and heavy undergrowth.

(*b*) *Tropical savanna climate:* Areas between the doldrums and trade wind belts: temperature not below 18°C, annual variation less than 12°C; dry season with less than 6 cm rain; vegetation of open grasslands with scattered trees.

(2) *Dry climates*

(*a*) *Steppe climate:* Pronounced wet and dry seasons, total precipitation less than 50 cm, with great variaton from year to year; evaporation usually exceeds precipitation; vegetation of short grasses.

(*b*) *Desert climate:* High summer temperature; usually very dry; large daily temperature ranges; only few rain showers.

(3) *Medium temperature-humid climates*

(*a*) *Warm climate with dry winter* (monsoon and upland savanna climate):

Wet summers; mean temperature of coldest month between +18° and —3°C; warmest month over 10°C.

(*b*) *Warm climate with dry summer* (mediterranean climate): Like (*a*) but reversed.

(*c*) *Humid temperate climate:* Ample rainfall throughout the year; temperature as in (*a*) and (*b*); cotton, wheat and corn producing areas of the world.

(4) *Cold humid climates*

(*a*) *Cold climate with no dry period:* Mean temperature of summer and winter 10°C and —3°C; precipitation throughout the year (*e.g.* great parts of Canada).

(*b*) *Cold climate with dry winter* (monsoon type): Temperature like (*a*); little rainfall in winter; only represented in N.E. Asia.

(5) *Polar climates*

(*a*) *Tundra climate:* Climate of the far North; mean temperature of warmest month less than 10°C; frozen soil throughout the year; only mosses and small bushes.

(*b*) *Ice cap climate:* Mean temperature of warmest month below 0°C.

Recently Thornwaite has introduced a new classification, in some aspects more satisfactory than Köppen's classification. Apart from temperature and precipitation it takes into consideration the degree of evaporation which depends on wind speed, humidity and temperature. Although none of the existing climatic classifications are satisfactory, the summary given clearly indicates that the biological effects, to be expected as a result of these entirely different climatic zones, will differ considerably.

On page 4 we mentioned the concept meteorotropism, the capacity of the living organism to register physiologically the external stimuli of the environment due to changes in weather and climate.

De Rudder [6, p. 34] introduced the concept *index of meteorotropism (M),* in order to indicate the degree of meteorotropism:

$$M = \frac{N \times K_n}{n \times K_N}$$

in which N=total number of days or hours observed, n=number of days with a specific meteorological disturbance (cold front, etc.), K_N=total number of observed meteorotropic events (*e.g.* beginning of a certain disease) and K_n=number of the same meteorotropic events observed during the number (n) of meteorologically disturbed days

According to De Rudder, in the case of pronounced meteorotropism the ratio of M is about 2. If M is smaller than 1 a *negative biotropic action* exists, *i.e.* the particular disease occurs only rarely during the selected weather condition. However, although meteorotropism is very likely if M is found to be 2, a statistical analysis must be made to determine whether the observed correlation is a matter of mere chance. Some of the methods used for this purpose in biometeorology are described on pp. 169–178.

A final important concept should be mentioned before closing this Part, *viz.*, the *morbidity limit*. The present author introduced this concept to indicate the specific physiological condition of a healthy person which leads to disease if this particular labile condition is surpassed. In other words, a certain unfavourable physico-chemical condition may prevail in the blood of an apparently healthy person but if, due to external meteorological stimuli, this physico-chemical condition is only slightly changed, the healthy state of a person may change into that of a diseased one. It is this physico-chemical boundary which represents the physiological limit above which a morbid condition may originate. This morbidity limit is different each day for different people and differs in the same person from one day to the other. This explains why the same meteorological triggering force may cause a disease in a particular person on a certain day, whereas in others no biological effects are observed. In the following chapters several examples of this principle will be discussed.

PART II

Principal Meteorological Factors to be Recorded and Instruments to be Used

CHAPTER I

Physical Factors

Section 1. Temperature

Temperature is a physical concept to measure the hotness (*i.e.* the total thermal energy) of bodies and the differences in thermal energy between different bodies. Whereas in physics and meteorology only one group of temperature recordings is studied, which could be described as *physical* temperature, in biological studies another type of temperature of the environment plays an important role, and this could be conveniently termed the *biometeorological* temperature.

Subsect. A. PHYSICAL TEMPERATURES

1. Characteristics of Physical Temperatures

The transfer of heat depends on four different physical mechanisms: conduction, convection, radiation and evaporation (and condensation). *Conduction* is defined as the flow of thermal energy (heat) through an unequally heated substance from places of higher to those of lower temperature. It is the main process of heat transfer in solids. *Convection* is a process of heat transfer in liquids or gases due to the flow of currents which carry the heat away. *Radiation* of heat is a form of electromagnetic energy transfer from one body to another without sensibly warming the intervening space. Both conduction and convection require matter for the heat transfer, whereas radiant heat can pass through a vacuum. *Evaporation* of a liquid on a solid surface requires heat which is taken from the surface of the solid, causing a cooling effect. *Condensation* of this fluid releases the heat required for evaporation causing an increase in temperature of the solid surface. In order to understand the physiology of heating or cooling of the living organism it is necessary to consider a number of important features of each of the abovementioned processes (for further details, see in particular the excellent reviews by Bedford, Yaglou and others [577, 790–793]).

Conduction

The rate of heat transfer through a solid body depends on a number of factors:

(1) The conductive power or thermal conductivity (k), which is defined as the number of gram-calories conducted per cm^2/per second, across two surfaces of a body 1 cm apart, per 1°C difference between these two surfaces.

(2) The difference between the temperatures of the lower and upper surfaces of the body.

(3) The surface area of the body.

(4) The thickness of the body: with a given temperature difference the rate of conduction decreases with increasing thickness.

As a general rule, good heat conductors (like metals) are good electrical conductors and *vice versa*. If the thermal conductivity of wood is taken as 1 the following differences in thermal conductivity are found [577, p. 9]: aluminium 1463, steel 334, bricks 8.0, glass 7.3, water at 20°C 4.15, cotton cloth 0,49, woollen cloth 0.29, air at 22°C 0.167. In other words air is a poorer conductor than most solids.

As a result, porous non-metallic substances, containing air in the pores, usually have very low thermal conductivities (lower than glass), *e.g.* cork 0.33, fibre-board 0.38. The same is true of air spaces in clothes and between the walls in houses. The impact on various biometeorological problems will be discussed later.

Convection

Increase in temperature in parts of a liquid or gas, due to conduction of heat from a solid to the liquid or air touching the solid surface, decreases the density of the liquid and gas. Cooler, denser parts of these liquids or gases will replace the lighter substances, creating currents known as *convection currents*. Such air currents increase the heat transfer from hot surfaces by convection.

Heat loss by air convection depends on a number of factors:

(1) It is proportional to the $^5/_4$th power of the *difference of the temperatures* of the object and that of the surrounding air.

(2) It depends on the *shape, size* and *orientation* of the object.

Bedford[577, p. 10] gave the following general formula used in thermal engineering calculations, mainly based on the publications of Griffiths and Davis[639]:

$$H_c = C\left(\frac{1}{D}\right)^{0.2} \cdot \left(\frac{1}{T}\right)^{0.181} \cdot \Theta^{1.27}$$

where H_c = heat transmission by convection in British thermal units/ft.^{2}/h (by multiplying by 0.0003445, c.g.s. units are obtained); C = constant depending on shape and orientation of the surface [for vertical surfaces

$C = 1.394$; for horizontal surfaces, facing upwards $C = 1.79$; for horizontal surfaces, facing downwards $C = 0.89$; for horizontal cylinders $C = 1.016$ (plates should be warmer than the air)]; D = diameter of pipe or height of the plane vertical surface in inches; T = mean of the temperatures of the surface and of the air in °F abs. (*i.e.* t °F+460); Θ = temperature difference in °F.

(3) It depends also on the *speed of a passing air stream* (so-called *forced convection*). The rate of heat loss increases with the air speed. It is directly proportional to the temperature difference multiplied by a velocity factor (v) depending on the size of the cooling body. For air flow parallel to fine cylindrical wires $v = 0.5$; for cylinders 25 cm or more in diameter it is about 0.7; for plane surfaces with parallel air flow and high air velocities $v = 0.8$.

It is generally known that at low temperatures thermal protection against cold is more difficult when humidity of the air is high. It has been always assumed that this effect of damp cold is due to the effect of humidity on thermal insulation of the clothing. However, Burton[598] demonstrated as far back as 1934 that there is *no appreciable difference in the non-evaporative heat loss of a warm body, like the skin, whether humidity is high or low,* provided that the temperature difference between skin and environment is the same in both experiments and also the degree of air movement.

Loss of heat by radiation, conduction and convection will be the same. The capacity of water vapour to carry away heat is almost equal to that of any other gas. Burton demonstrated the above statement as follows: 1 l of dry air at 10°C (18°F) weighs 1.342 g; specific heat of dry air = 0.240 cal/g; the thermal capacity of 1 l dry air = $1.342 \cdot 0.240 = 0.322$ cal/l. Air saturated with water vapour at 10°C, contains 0.0093 g of water vapour. Specific heat of water-saturated air = 0.48 cal/g. Thermal capacity of 1 l air = $0.0093 \cdot 0.48 = 0.0045$ cal. Density of saturated air = 1.2423 g/l (*i.e.* 10% less than dry air). Apart from water vapour there is 1.2330 g of dry air with thermal capacity of $1.2330 \cdot 0.24 = 0.2953$ cal. Total thermal capacity of 1 l of saturated air at 10°C = $0.2953 + 0.0045 = 0.2998$ cal. This is 7% less than of dry air. If studied per gram of air, the thermal capacity of 1 g of dry air at 10%C = 0.240 cal, of saturated air 0.241 cal. So the thermal capacity of moist air per gramweight is not greater than that of dry air. As convection accounts for less than half of the total heat loss, the total heat loss with high humidity cannot be more than 5% greater at most.

Radiation

The intensity and wavelengths of the electromagnetic thermal waves emitted by heated bodies depend on the substance and temperature of the body.

According to the law of Stefan-Boltzmann, the total energy *(H_R)* radiated by a perfectly "black body" (*i.e.* a completely opaque, non-reflecting body surface) per unit time, per unit area of surface, is given by the following formula:

$$H_R = {}^{\sigma}T^4$$

where T = absolute temperature of the surface in °C; σ = Stefan's constant = $1.36 \cdot 10^{-12}$ cal/cm^{-2}/sec^{-1}/degree^{-4}. In the case of an imperfectly black body, the amount of radiated energy is less for each wavelength (law of Kirchhoff). A bright tin surface radiates only 12% of that of a lamp-black surface.

Wien observed two phenomena, with rising temperature of the body:

(1) *The wavelength of maximum radiation intensity* (λ_m) *becomes shorter.* In other words: more energy is radiated as shorter electromagnetic waves. This wavelength-temperature relationship is indicated in the displacement law of Wien:

$$\lambda_m T = 0.52$$

where λ_m = wavelength with maximum emissive power in cm; T = absolute temperature in °F.

(2) *The intensity of* λ_m *is proportional to the fifth power of the absolute temperature.* Therefore the intensity increase with rising temperatures for longer waves as well. For different wavelengths the energy radiated by a perfectly black body can be calculated by the Planck's formula:

$$E_\lambda = \frac{C_1}{\lambda^5 \cdot (e^{C_2/\lambda T} - 1)} \text{ ergs/cm}^2\text{/sec}$$

where λ = wavelength in cm; T = temperature of radiating surface in °C abs.; e = base of Napierian logarithms; C_1 = a constant = $4.933 \cdot 10^{-15}$ and C_2 = another constant = 1.432.

Good emitters of heat radiation are also generally good absorbers, while poor emitters are poor absorbers but good reflectors (many bright metals). Most building materials are usually good absorbers and poor reflectors of heat. Griffiths and Davis[639] were able to demonstrate that at room temperatures various paints do not differ much in heat radiation, but for solar radiation the emitted energy varied considerably (97% for dark blue and black against 12–14% for white paints). As building materials are good absorbers in a well-heated room (21°C = 70°F), a chair near a cold brick wall may cause great discomfort to a person with a body temperature of 37°C sitting in it. Even with a two-layer brick wall with an air space in between, as is customary in the Netherlands, on cold days the wall temperature may be 13°C (56°F), whereas the air temperature everywhere in the room is 21°C.

The exchange of radiant heat energy between a body and its surroundings is determined by the equation

$$H_R = \sigma E\ (T^4{}_1 - T^4{}_2)$$

in which E = emissivity of the body; T_1 and T_2 = absolute temperatures of the body and surroundings resp., expressed in °F. abs.; σ = Stefan's constant (see above); H_R = heat exchange by radiation.

Clothing and the human skin radiate almost like black surfaces.

In the example given, $T_1 = 37°C$, $T_2 = 13°C$ if our back is close to the wall, whereas for the front part of the body facing the room $T_2 = 21°C$. Needless to say, a considerable difference in heat loss occurs on both sides of the body which creates this feeling of discomfort, the physiology of which will be discussed on p. 230. Whereas, in view of the wavelengths usually encountered, indoors white clothing has no advantage over black, outdoors in the sun white clothes reflect most of the sun's radiation while it still radiates heat outwards. Black clothes would absorb the sun rays. This scientific fact corresponds to the empirical knowledge of many native inhabitants of desert countries that their body should be covered in the sun, preferably with white linen clothes. Arab women of the desert Bedouin probably took to wearing black as the result of old social or religious customs or the availability of material rather than for physiological reasons (see p. 434). The black tent absorbs heat at a distance.

Evaporation

The amount of water evaporating from a wet surface into the air depends mainly on the difference between the partial pressure of the water vapour of the wet surface and that of the air immediately adjacent to it. The pressure of water vapour in the air is part of the total atmospheric pressure. It varies with the amount of vapour in a given volume of air and the temperature. The maximum partial pressure of water vapour increases with increasing temperature.

The air film close to the wet surface is usually nearly saturated with vapour in contrast to the air further away. There will consequently be little evaporation unless air movements replace the saturated air by drier air. As a result, more water is evaporated from the wet surface (*e.g.* our skin), which requires energy and therefore lowers the temperature of the surface till an equilibrium is reached in which the heat gained by convection and radiation is balanced by the loss of heat. Studies by Powell and Griffiths[729, 730] have shown that the rate of evaporation and, therefore, the cooling effect, is more complicated than indicated above. It actually depends on at least 5 factors summarized by Badford[577, p. 19]:

(1) The geometrical form of the surface: (*i*) per unit area evaporation of cylindrical bodies increases with decreasing diameter and (*ii*) evaporation rate from a plane horizontal surface is considerably less than from a cylindrical surface. This is of importance if different human bodies and different parts of the same body are compared.

(2) The nature of air flow over the surface.

(3) The velocity of air relative to the surface.

(4) The difference between the partial water vapour pressure (corresponding to the temperature) of the surface and the actual water vapour pressure in the air stream.

(5) The resistance to the flow of water from the interior of the body to the surface.

On page 215 we shall revert to this important problem.

2. *Instruments Used for Recording of Physical Temperature*

For biometeorological studies, accurate recording is required of the daily changes in temperature. Continuous automatic recordings are required from which, in particular, the *daily maximum, minimum* and *average temperatures* are determined, three important data for a meteorological analysis of clinical phenomena.

The various instruments used for recording conduction and convection heat are usually based on either one of the following principles:

(1) *The expansive effect of heat.* The *mercury thermometer* utilizes the fact that mercury has little specific heat and therefore reacts to small changes in temperature. It has, moreover, a fairly constant expansion coefficient and high boiling point. It can be used for temperatures above —39°C. For lower temperatures alcohol or toluol can be used. Another type based on the expansion principle is the *bimetallic strip.* It consists of 2 metal strips with different linear coefficients of expansion which are welded together at one end. The other end curves as a result of temperature changes having different effects on both metals. With a number of small mechanical linkages, the change in curvature is transmitted to a pen moving along a rotating chart. The readings are regularly checked against a standard mercury thermometer. This bimetallic thermometer is often used in combination with a hygrometer known as *thermo-hygrograph.* A similar principle is used in the *Bourdon tube thermograph,* which consists of a curved, flattened tube, completely filled with an organic fluid. As the cubic expansion coefficients of fluid and

metal are different, the tube becomes deformed with changes in temperature. By using special constructions built into the stem of U-shaped mercury thermometers, *maximum* and *minimum temperature recorders* are obtained.

(2) The *change in pressure or volume of a gas due to change in temperature.* Either the *constant pressure gas thermometer* or the *constant volume gas thermometer* is used. The latter uses the principle that at a constant volume the pressure of a gas is directly proportional to the absolute temperature.

(3) The *change in electrical resistance in a wire.* In the *resistance thermometers* ("thermistors", an abbreviation of the name "thermal sensitive resistor") this change is recorded with an ohmmeter as a function of temperature. In the *thermojunction* or *thermocouple thermometer* the thermocouple is made, for example, of a constantan and copper wire soldered together. Due to temperature changes, electromotor forces are developed at the contact point of the metals, the potentials being recorded by a potentiometer. Hot and cold junctions may differ 50 or more $\mu V/°C$ difference.

(4) The *change in wavelength of radiation emitted by hot bodies.* These changes are measured by optical pyrometers. They are mainly used for very high temperature recording.

Whereas the first group of expansion thermometers is very common in outdoor meteorological stations, the bimetallic strip type in particular, the third group is used more especially in biometeorological work. The electric types are very popular, above all if accurate microclimatic studies are made with continuous recording at a certain distance from the measured environment.

The thermometers for meteorological recordings are usually placed in a specially built meteorological shelter, a wooden hut above the ground with sufficient openings for the air to circulate. It protects the thermometer against strong wind turbulence and precipitation. The hut should be high enough above the ground for differences in composition and vegetation of the soil not to affect the recordings unduly. It should be sufficiently far away from neighbouring buildings, smoke producers or spray causing water masses.

Biometeorological work likewise involves also measuring the direct mean heat radiation of the environment. *Radiation thermopiles* have been developed for this purpose connected to a sensitive galvanometer. For indirect measurements a rather singular instrument is used, known as a *globe thermometer,* which consists of a hollow copper sphere of 6–8 inches diameter coated with black paint. It contains a mercury thermometer at the centre of the sphere. The globe temperature is affected by the air velocity. The greater the velocity, the nearer does the globe temperature approach the air temperature.

If the radiating body is warmer than the mean radiant temperature of the air the heat radiation gain (H_R) of the globe thermometer can be calculated with the aid of the formula given by Bedford[577, p. 38]:

$$H_R = 0.95 \cdot 1.73 \cdot 10^{-9} \cdot (T_A^4 - T_G^4)$$

where T_A = mean radiant temperature of the air in °F abs. and T_G = temperature of the globe thermometer in °F abs.

A direct radiation device was developed by Bedford and Warner[579] using a *Moll thermopile*. However, in recent years an excellent instrument has been designed by Hardy[643], who published a series of studies on direct radiation measurements[643-658]. The *Hardy dermal radiometer,* originally developed in 1934, was improved and described in 1952 (ref.[651]). Instead of a potentiometer circuit, a Weston millivoltmeter is used together with a thermopile for the actual radiation reception. The latter consists of eight bismuth-antimony, bismuth-tin thermocouples, connected in series. The warm junctions are welded to tin foil radiation receivers, blackened with bismuth black. An aluminium cone in a bakelite barrel is mounted in front of the thermopile. It is evident that the instrument must be calibrated first against a black body radiator over the various ranges of temperature in which it is to be used. Since this instrument was developed biometeorological radiation studies of living organisms have been considerably facilitated.

Another group of thermometers measures the degree of evaporation of the thermometer as a function of the humidity of the air. These so-called *wet- and dry-bulb thermometers* consist of two thermometers: one ordinary dry-bulb mercury thermometer which measures the temperature of the air and one with the bulb covered with wet muslin. If the air is completely saturated with water vapour, the temperatures recorded by both thermometers will be the same. Otherwise, due to evaporation, the wet-bulb temperature will always be lower. The drier the air, the greater the difference between the two temperature readings.

Subsect. B. BIOMETEOROLOGICAL TEMPERATURES

1. *Characteristics of Biometeorological Temperatures*

Whereas in physical and meteorological studies the thermal environment is usually characterized only in terms of average air temperature determined by temperature and humidity, for biological studies it is insufficient and a socalled *biometeorological temperature index* is required in order to indicate the degree of thermal comfort.

As far back as 1733 it was pointed out by J. Arbuthnot in his *Essay concerning the Effects of Air on Human Bodies,* and further stressed in 1804 by J. Leslie *An Experimental Inquiry into the Nature and Propagation of Heat*) that the exposure of a body to air movement changes the entire heat balance considerably. Since than, various new concepts have been introduced to register the *biological temperature* of an environment.

Effective temperature of Houghten and Yaglou

This concept was introduced by Houghten, Yaglou and Miller[679] in 1923 and is defined as the temperature of still air saturated with water vapour, in which subjects experience an equivalent sensation of warmth. These empirical subjective values were determined at different temperatures in a long series of experiments in so-called "climatic chambers" in the laboratory of the American Society of Heating and Ventilation Engineers at Pittsburg (U.S.A.). Two scales of effective temperatures were determined, one for persons stripped to the waist (known as basic scale) and another for people normally clad (the normal scale). The air velocity should be taken into consideration in addition to the air temperature and humidity. In a number of effective temperature nomograms the effect of air velocity on human comfort is given, but the radiation effect was ignored.

Although the effective temperatures are subjective values for different degrees of warmth, it has been possible to demonstrate that these values correlate with physiological reactions such as pulse rate, body temperature, etc.

In 1955 E. C. Thom (Chief of the Special Projects Section of the Office of Climatology, U.S. Weather Bureau) introduced a special, empirically determined *temperature-humidity index* (T.H.I., until recently called discomfort index). Its main purpose was to have a simple method of determining the effect of summer conditions in the U.S.A. on human comfort[766-769].

Three linear equations were developed by J. F. Bosen (of the Office of Climatology, U.S. Weather Bureau) which have given very satisfactory results for the specific weather conditions during summer in the U.S.A. and correspond fairly well with the nomogram data of Yaglou:

$$\text{T.H.I.} = 0.4\,(T_d + T_w) + 15$$
$$\text{T.H.I.} = 0.55\,T_d + 0.2\,T_{dp} + 17.5$$
$$\text{T.H.I.} = T_d - (0.55 - 0.55\,\text{R.H.})\,(T_d - 58)$$

where T_d = dry-bulb (air) temperature in °F, T_w = wet-bulb temperature, in °F, T_{dp} = dew point temperature in °F (dew point is the temperature to which a sample of air must be cooled to become saturated with water vapour causing dew formation; see page 47); R.H. = relative humidity in %, *i.e.* in the equation R.H. is used as a decimal, in other words 50% relative humidity is indicated as 0.50.

Empirical studies by Thom and others have shown that in the U.S.A. for 10% of the population life becomes unpleasant when the discomfort index reaches 70. Fifty per cent of the population begins to suffer if T.H.I. reaches 75. At 79 everybody is most uncomfortable, at 86 Government offices at Washington D.C. may close. In New England, which is much cooler in summer (T_d = 85, R.H. = 60), discomfort is reached at T.H.I. = 79. Along the Great Lakes a temperature of 85 and R.H. of 50 makes life uncomfortable. In the arid states of Arizona the discomfort boundary is reached only if T_d = 98°F and R.H = 30%. These are outdoor criteria, where there is always some air circulation. Indoors the discomfort boundary may be reached 3–5 points earlier.

In the equations of Thom and Bosen the radiation and air movement are neglected for two practical reasons. There is usually a rather high correlation between temperature and radiation, so the temperature effect of radiation is already taken into consideration. As most American citizens spend a great part of their time in buildings with little air movement, the effect of this factor can also often be neglected. However, it has been suggested by others that the radiation-wind speed effect should be introduced by using a different value for the dry-bulb temperature T_d. The mean radiant temperature of the environment as a function of air velocity (T_{RV}) can be determined with the help of the formula given by Bedford[577, p. 38]:

$$T^4_{RV} \left\{ T^4_G \cdot 10^{-9} + 0.1028 \sqrt{V} \cdot (T_g - T_A) \right\} \cdot 10^9$$

where T_g = temperature of the globe thermometer in °F; V = air velocity in ft./min; T_G = temperature of the globe thermometer in °F abs. = T_g + 460; T_A = temperature of the air in °F.

Equivalent temperature of Dufton

This concept was introduced by Dufton[611] in 1929 to include the effect of radiant heat which was neglected in the Effective Temperature concept; on the other hand, in Dufton's concept the effect of humidity is neglected. Dufton constructed a special instrument, the *eupatheostat*[610] (with a surface temperature corresponding with that of the human body during comfortable conditions), which will be described further on in this Section. In a later development[614] in 1936, the surface temperature was identical with that of the clothed human body over a range of environmental temperatures. The equivalent temperature of the revised instrument was defined by Bedford[577, p. 50] as follows: "The E.T. is the temperature of a uniform enclosure in which, in still air, a black body of sufficient size would lose heat at the same rate as in the environment, the surface temperature of the body being 1/3 of the way between the temperature of the enclosure and 100°F".

The equivalent temperature (T_{Eq}) can be measured directly with the eupatheostat, as indicated above, but it can also be estimated by measuring individual thermal factors as described by Bedford[576] in 1936. Two formulas were developed, based on an experimental study of thermal comfort:

$$T_{Eq} = 0.522\, T_A + 0.478\, T_S - 0.01474 \sqrt{V}\,(100 - T_A)$$

where T_A = temperature of the air in °F (measured with a dry-bulb thermometer); T_S = mean temperature of the surroundings in °F; V = velocity of the air in ft./min.

A second formula gives T_{Eq} in relation to the temperature of the globe thermometer (T_g) in °F:

$$T_{Eq} = 0.522\, T_A + 0.478\, T_g + \sqrt{V}\,(0.0808\, T_g - 0.0661\, T_A - 1.474)$$

The radiation-convection temperature of Vernon

In 1930 Vernon[774] introduced this concept for a globe thermometer-temperature as a means of indicating the combined effects of radiation and convection on the human body. As explained by Bedford[577], this temperature is inadequate as a comfort index because, if air and surrounding surfaces are at the same temperature, irrespective of air velocity, the globe thermometer will record the same air temperature only. However, for studies in closed rooms with little air movement the globe thermometer is a valuable temperature comfort index.

Resultant temperature of Missenard

An identical method was applied by Missenard[715] in 1935. He speaks of a resultant dry temperature and developed in 1933 and 1944 formulas[714, 716] for an improved "effective temperature", which takes into consideration air temperature, humidity (ignored by the equivalent temperature concept), radiation (ignored by the effective temperature concept) and air movement. As the calculations are rather laborious, Missenard constructed a number of nomograms from which the resultant temperature can be quickly determined.

2. *Instruments Used for Recording of Biometeorological Temperature*

Katathermometer

This instrument was introduced by Hill[676] in 1914. It can be used to determine the actual cooling power as a function of temperature, humidity and air velocity and as wind speed meter (anemometer).

The present-day Fuess katathermometer is a red alcohol thermometer with a bulb 4 cm long and 2 cm in diameter. On the vertical stem above the bulb there are two graduations 3°C apart. The upper mark represents the temperature scale 38°C, the lower 35°C. A point halfway between these two marks represents the average body temperature (36.5°C). At the top of the stem the bore is enlarged to form a small reservoir. After immersing the bulb in hot water (between 50° and 70°C), first the air bubbles must disappear and finally the alcohol reaches the upper reservoir. The bulb is carefully dried and the thermometer suspended in the air. The alcohol will fall and the time in seconds for the alcohol meniscus to pass the distance between the two marks on the stem is determined with a stop-watch. Four observations should be made and of the last three the average value is calculated. The katathermometer constant is of the order of 500 mcal/cm². This constant is divided by the number of seconds mentioned above. This quotient, the *cooling power,* gives the rate of heat loss from the bulb in mcal/cm²/sec.

The same is repeated with the bulb covered by a small wet muslin socket. This gives a better value for the cooling power of a wet skin. The wind speed V can be determined by the formula:

$$V = \left\{ \frac{\dfrac{H}{(T - t)} - a}{b} \right\}^2 \quad \text{(in ft./min)}$$

where H = cooling power (= Kata factor divided by cooling time in sec); T = constant of the bulb surface depending on the cooling range in °F; t = air temperature in °F; a and b = instrument constants depending on the general rate of air velocity, *i.e.* below or above 1 m/sec.

Globe thermometer

This instrument for radiation measurements was described on p. 39. In the various formulas given above it is also necessary to know the wet-bulb and dew-point temperatures. The determination of the former has already been described (wet- and dry-bulb thermometer). The *dew point* can be measured directly, using a *dew-point hygrometer,* or can be obtained indirectly by using a *dry- and wet-bulb thermometer* and *psychrometric tables.* The same ables can be used if the temperature and relative humidity are known. A well-known instrument is the *Regnault's hygrometer*. It consists of two tubes with thermometers, one of them having a polished silvered thimble at the bottom and being half-filled with ether. The silvered tube is connected with an aspirator which causes the ether to evaporate. As a result of the cooling, mist forms on the silvered thimble at the dew point, which can be read on the thermometer.

A simpler method is to fill a glass with water of room temperature. Small pieces of ice are added to the water and the moment the glass fogs up, the temperature is read from a thermometer placed in the water. Another similar simple method is to cover the bulb of an ordinary thermometer with cotton cloth, which is dipped in water. By placing the bulb in front of an electric fan, the temperature falls rapidly to the dew-point temperature which remains constant for some time.

Eupatheostat

This instrument was developed by Dufton in 1932 for equivalent temperature readings (see p. 42). It consists of an electrically heated, blackened copper cylinder, 22 inches high and $7^1/_2$ inches in diameter, the temperature being controlled by a thermostat. At a temperature of 78°F the heating current is cut off and as soon as the thermostat cools below 78°F the current is switched on again. This temperature was taken because, in a still air enclosure of 65°F, the surface temperature of a clothed human body is about 75°F.

The rate of heat loss of the eupatheostat and therefore the electric heat input, varies with temperature, air velocity and radiation of the environment and can be recorded automatically.

In later years Dufton changed this instrument into two katathermometers, one with a black, the other with a silvered bulb.

On p. 43 two formulas were given which enable us to calculate the equivalent temperature by measuring the globe thermometer temperature.

In the previous pages an extensive review is given of the various concepts and methods of recording temperature, which may seem rather long to many medical readers. However, it will be demonstrated in the next chapters that a substantial number of the meteorotropic phenomena are related to thermoregulation phenomena in the human body and, unless the environmental heat balance can be accurately recorded, biometeorological research on the human thermal balance cannot be very productive.

Section 2. Humidity

In the foregoing the humidity concept has been enlisted without being properly defined. Let us, therefore, now consider this physical factor. Humidity is a term describing the moisture content of the air. This concept can be used in various ways.

Relative humidity and water vapour pressure

It expresses the degree to which the air is saturated with moisture, perfectly dry air having a relative humidity of 0%, saturated air 100%. The saturation point depends on the temperature which affects the water vapour pressure (see p. 37). According to Dalton's law, in a certain volume of a mixture of gases the total pressure equals the sum of separate pressures each gas would exert if it occupied the same volume alone at the same temperature. The *partial water vapour pressure* in the atmosphere varies between 0 and 4% of the total atmospheric pressure. An interesting fact of vapour pressure is that it is independent of the presence of other gases. Therefore the pressure of a saturated vapour above a liquid will depend only on the temperature and the nature of the liquid, but not on the presence or absence of other gases.

The relative humidity R.H. $= P_a/P_s \cdot 100$, where P_a = actual vapour pressure and P_s = saturated vapour pressure.

The difficulty of the R.H. concept is that it is greatly affected by temperature. A very dry room with 29% R.H. and a temperature of 70°F could therefore become highly saturated by decreasing the temperature to 38°F, without any further changes in the environment (R.H. = 100%). For comfort studies we may be interested in the degree of dryness only, but for other biometeorological problems we may want to know the actual changes in the moisture content of the air.

Hair hygrometers, in which variations in the length of human hair, brought about by changes in humidity, are transmitted through a mechanical linkage to a pen moving over a rotating chart, are used for accurate measurements of the R.H. Unfortunately, they become inaccurate at low temperatures. In recent years a new accurate, but very expensive, instrument has been developed by the U.S. Weather Bureau, known as *infrared absorption hygrometer.* It is based on the principle that infrared radiation of 1.4μ wavelength is strongly absorbed by water vapour.

The water vapour pressure is usually not determined directly, but could be obtained with the aid of the formula for the R.H. just given. If we know the R.H. and the air temperature with tables giving the value of P_s as a function of temperature, P_a can be calculated (expressed in mm Hg or millibars; see p. 48). *E.g.*, for a temperature of 13°C and R.H. = 43%, P_s = 14.97 millibar; $P_a = \frac{43 \cdot 14.97}{100} = 6.44$ millibar.

Dew point

This concept was described on p. 41. The advantage of this concept is that, as long as air remains unsaturated and even with considerable changes in pressures, the dew point remains unchanged. As indicated on p. 44 the dew point can be determined by hygrometers and psychrometers.

Absolute humidity

This gives the water content in g/m³ of moist air. However, here again, as temperature affects volume, temperature will also affect this absolute humidity concept.

Specific humidity

It indicates the number of g of water/kg of *moist air*. The specific humidity (S.H.) is estimated with the following equation:

$$\text{S.H.} = \frac{622\, P_a}{P_{At}}$$

where P_a = actual water vapour pressure (to be determined by the formula of R.H. given above); P_{At} = total atmospheric pressure. In the exampie given P_a = 6.44 millibar; with P_{At} = 980 millibar, S.H. = 4.08 g H_2O/kg moist air.

Mixing ratio

Another important humidity concept is the "mixing ratio" (M.R.). It is the number of g of water/kg of *dry air*.

$$\text{M.R.} = \frac{622\, P_a}{P_d}$$

where P_d = partial pressure of dry air = total atmospheric pressure minus P_a. In other words

$$\text{M.R.} = \frac{622\, P_a}{P_{At} - P_a}$$

As P_{At} is usually more than 100 times larger than P_a, the difference between S.H. and M.R. is usually less than 1%. Both are therefore convenient concepts in biometeorological work.

Section 3. Atmospheric Pressure

The atmospheric pressure is measured either in cm/cm², in mm/cm² or in *millibars* (equal to $^{1}/_{1000}$ of a bar). The term *bar* was introduced in 1906 by V. Bjerknes and J. W. Sandström.

By definition a bar represents the pressure of one million dynes/cm², which is about the normal surface pressure at sea level, equal to the pressure of a mercury column 76 cm high which is equal to a weight/cm² of $76 \cdot 13.596$ g Hg = 1033.3 g. The actual conversion values are: 760 mm = 29.921 in. = 1013.25 millibars = 1 atm. = $76 \cdot 13.596 \cdot 981$ or 1,013,250 dynes / cm². In other words, about a million. It is for this reason that a millibar was defined as 1000 dynes/cm². Lines connecting points of equal pressure are called *isobars* (Fig. 2).

Influence of latitude

As the acceleration of gravity (about 980.6 cm/sec²) varies with *latitude,* two points on earth with the same barometric pressure may still differ in actual pressure. For example, 750 mm Hg represents at the equator 997.3 millibar (mb), at 45° latitude 999.9, at 80° latitude 1002.3 mb.

The barometric pressure in mm can be converted by the formula:

$$B_{45} = B_{\varphi} \frac{g_{\varphi}}{g_{45}}$$

where B_{45} = barometric pressure reduced at 45° latitude (999.9 mb); B_{φ} = observed barometric pressure at latitude φ; g_{φ} = acceleration of gravity at latitude φ; g_{45} = acceleration of gravity at 45° latitude.

Influence of altitude

Barometric pressure also changes with height. If the temperature of the air does not change appreciably with the elevation, the following formula can be used to determine the decrease in barometric pressure with increasing altitude:

$$\log P = \log P_o - \frac{H - H_o}{18400 - (1 + \alpha T_m)}$$

where P = barometric pressure at the elevation H; P_o = barometric pressure at the elevation H_o; T_m = average temperature in the interval between H and H_o; α = expansion coefficient of gas (0.00366).

The fall in barometric pressure is about 1 mm per 10.5 m rise in elevation. If the barometric pressure at sea level is 760 mm, the approximate value at 1 km altitude is 674 mm, at 2 km 596 mm, at 3 km 526 mm, at 4 km 462 mm, at 5 km 405 mm and at 10 km 191 mm.

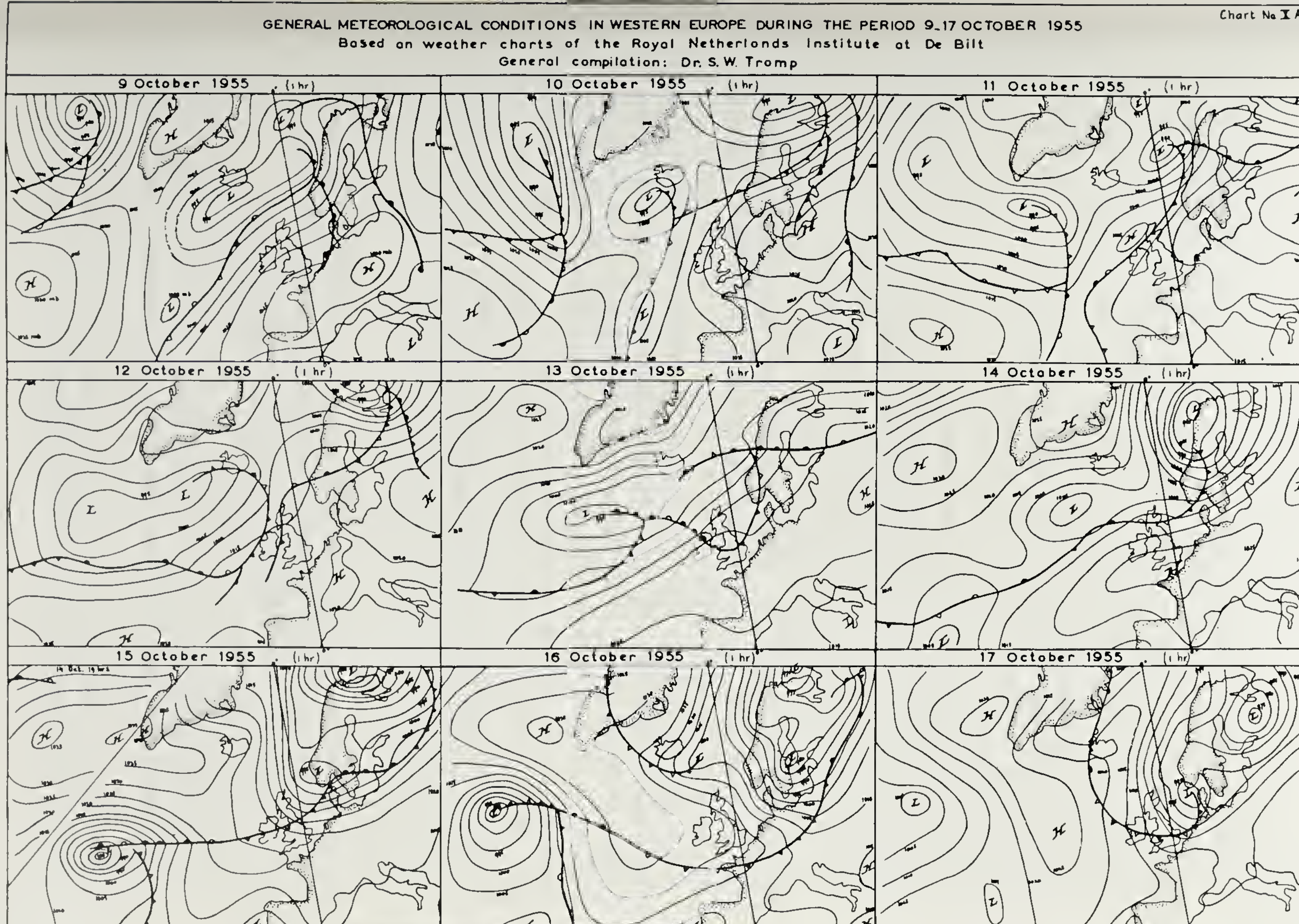

Fig. 2. General meteorological conditions in W. Europe during the period 9–17 October 1955, indicating the rapidly changing patterns of isobars.

Influence of temperature

Due to the temperature effect (see formula p. 48), in summer (with high temperatures) the barometer will indicate elevations which are too low, in winter they are too high. A 5000 m reading could be 5300 in summer, against 4900 in winter. In other words the atmospheric pressure decreases more slowly in a vertical column of warm tropical air than in one of cold polar air. At 5000 m the difference in pressure would be 547 mb (warm) against 534.9 (cold). This difference in pressure causes air movements.

Daily rhythms

(1) The atmospheric pressure has a daily rhythm as a result of the heating of the air by the sun, which is particularly pronounced at low latitudes. Maximum pressures occur at 10 and 22 hours, minimum at 4 and 16 hours. The amplitude in the tropics is 3–4 mb, in northern regions about 0.7 mb.

(2) The atmosphere also exhibits tidal phenomena. As a result of the attraction of the sun, a progressive wave follows the sun from east to west with crests near 10 and 22 hours local time. The amplitude of the solar tide is 1.3 mb at the equator and vanishes at the poles. The lunar tide causes differences of 0.09 mb only.

(3) Irregular changes due to approaching depressions surpass these daily effects considerably. In the tropics the daily disturbances are usually small; at greater latitudes they can be considerable (up to 120 mb or 90 mm). However, as a rule in N.W. Europe the fall in barometric pressure in 24 hours does not exceed 30 mm. During the heavy storm of October 1959 the B.P. fell by 43 mm in 3 days, on 12th Dec. 1958 about 40 mm in 10 days; as a rule the amplitude of the daily fluctuations does not exceed 10 mm. However, in the Caribbean area or near Japan considerably larger fluctuations are observed.

Recording

The barometric pressure is either recorded by a *mercury barometer* or by non-liquid *aneroid barometers,* which use the change in shape of an evacuated, elastic metal cell, resulting from changes in atmospheric pressure. *Aneroid barographs,* incorporating a pen moving over a graduated chart placed on a revolving drum, are used for permanent recording. A third type of instrument is the *hypsometer,* using the principle that a fluid boils as soon as the vapour pressure equals atmospheric pressure. Pure water at sea level boils at 100°C (760 mm Hg), at 2940 m at 90°C (526 mm Hg), with an average of 0.037°C per 1 mm pressure change. By measuring the boiling point accurately, the atmospheric pressure can be deduced from a table. The instrument is not very accurate, because very exact temperature measurements are required. An *"ether hypsometer"* with a temperature accuracy of 1°C has a pressure accuracy of only 35 mb.

We have discussed the various barometric phenomena at some length because a considerable number of papers have been published on the direct influence of changes in atmospheric pressure on human health. As we have seen above, with deep depressions passing over W. Europe, the actual pressure decrease on our skin as a rule does not exceed 30 mm Hg = $3 \cdot 13.6 \cdot 981$ dynes/cm². Of greater importance is the fact that, although the composition of the atmosphere is not affected by altitude, the O_2 pressure of inspired air is reduced proportionally to the decrease in total atmospheric pressure (see p. 293).

Section 4. Wind (Speed and Direction)

Wind speed formula

We have seen that, due to temperature differences on earth, pressure differences are created in the atmosphere which lead to air currents and wind. As a result of the rotation of the earth (Coriolis force), the direction of the wind does not connect the centres of high and low pressure but deviates to the right in the northern hemisphere (see p. 21). Above 20° latitude the speed of the wind along a straight line can be calculated with the aid of so-called *geostrophic wind formulae,* in which acceleration and frictional forces are ignored:

$$\text{wind speed } V_1 = \frac{1}{2\omega \cdot \sin\varphi \cdot \rho} \cdot \frac{d_p}{d_n}$$

where ω = angular velocity of the earth's rotation in radians/sec = $7.29 \cdot 10^{-5}$; φ = latitude; ρ = density of the air = 0.0011 g/cm³; d_p/d_n = pressure gradient = pressure difference in mb divided by the distance in km.

For

$$\varphi = 30^\circ$$

$$\frac{d_p}{d_n} = \frac{3 \text{ mb}}{100 \text{ km}}$$

$$V = \frac{1}{2 \cdot 7.29 \cdot 10^{-5} \cdot \sin 30^\circ \cdot 0.0011} \cdot \frac{3000}{100 \cdot 10^5} = 3730 \text{ cm/sec} =$$

$$= 83.4 \text{ miles/h}$$

As a rule the air flow follows not straight but curved lines. In the case of cyclonic (low pressure) flow the wind speed can be calculated by the *gradient wind speed formula*:

$$V_2 = \sqrt{\frac{1}{\rho} \cdot \frac{d_p}{d_n} + (r\omega\sin\varphi)^2} - r\omega\sin\varphi$$

where r = radius of the curvature of the air flow. With r = 200 km = d_n and d_p = 3 mb, V_2 = 25.4 miles/h. The same applies in cases of linear flow V_1 = 41.8 miles/h. In other words *cyclonic flow is always smaller than straight-line flow,* anticyclonic flow is always larger. However, the winds near the centre of anticyclones, where the radius of curvature is usually small, are always light, in contrast to the cyclonic areas.

On p. 26 we discussed the differences between sea, land, valley and mountain breezes as a result of temperature contrasts on the surface of the earth; also, briefly, the significance of jet streams.

The *wind speed* can be expressed in m/sec, km/h or sea miles/h or in knots (1 sea mile = 1 sec of the meridian = $^1/_{60} \cdot 111.1$ = 1.85 km. 1 knot is the speed of one sea mile/h = 0.51479 or roughly $^1/_2$ m/sec). If no instruments are available the wind speed is usually expressed in the *scale of Beaufort* (introduced by the English Admiral Sir Francis Beaufort in 1804), which describes the effect of the wind force on the surface of the earth; this force $F = 0.075\ V^2$ kg/m² in which V = wind speed in m/sec. For example: with a Beaufort scale 0: smoke rises vertically, with no perceptible movement of anything (wind speed less than 0.2 m/sec.). With a scale 5: large branches and small trees in leaf begin to sway and crested wavelets form on inland water (wind speed 8.0–10.7 m/sec).

Measuring devices

The *wind direction,* always given as the direction from which the air is blowing, is recorded with different types of *wind vanes* the position of which is electrically recorded in automatic recording devices.

The *wind speed* is recorded in different ways. For meteorological purposes a three or four cup revolving device is used connected with a recording apparatus, known as a *Robinson anemometer.* Certain devices use the pressure of wind acting on a tube facing into the wind or the cooling effect on a hot wire. For very accurate measurements of low speeds in buildings the *katathermometer* has been used (see p. 44) In recent years an excellent laboratory instrument has been developed, known as the *anemotherm air meter,* measuring air velocity as low as 5 cm/sec up to 40 m/sec. At the same time it can be used as a temperature recorder for temperatures from —30 to +125°C with an accuracy of $^1/_2$°C. It is based on the principle used in the original pressure tube of Dines, which consists of a horizontal pressure tube placed by a vane in the direction of the wind. The pressure increase is accurately recorded by a special device.

The *wind pressure* can be calculated, but also directly measured, for example with *Wild's wind plate,* a rectangular plate swinging along a horizontal axis, which is always kept perpendicular to the wind by a wind vane on top of this axis.

The biological importance of the accurate recording of air velocity was fully discussed in the previous section on temperature recording. As wind is one of the most important factors affecting the cooling effect of the environment on the human body, it is evident that in biometeorological studies a careful analysis of this factor is necessary.

Section 5. Condensation and Precipitation

Condensation occurs in the atmosphere as soon as the air is cooled below the saturation temperature (dew point) or if water vapour is added to fairly saturated air. A considerable amount of heat is liberated during the change from the vapour state to water. At 20°C it amounts to 585 calories per gram condensed. From liquid to solid (ice) another 80 calories are liberated. The direct transfer from vapour to solid is known as *sublimation*. Whereas condensation can start at relative humidities under 100%, sublimation requires supersaturation.

Condensation and sublimation usually require solid particles, *e.g.* grass on the ground (causing dew or frost) or nuclei in the air. The latter are divided into two groups: *sublimation* and *condensation nuclei*. The *sublimation nuclei* usually consist of microscopic inorganic particles of minerals or rocks. The *condensation nuclei* (size 0.01–50μ) are composed of small salt crystals, droplets of sulphuric acid, smoke particles, etc. (see also p. 115), the number varying from a few hundred to several millions per cm^3. This accounts for the common occurrence of condensation and fog around cities, where the nuclei count may exceed 100,000. They are often hygroscopic and begin to absorb water at relative humidities of 80%. The process is hastened by a fall in temperature (*e.g.* on a cold night with clear sky and strong radiation) or by constant temperature when dry air from the continent moves to the ocean and, due to gradual evaporation of ocean water, the amount of water vapour in the air is increased. In both cases fog will be formed.

Perfectly clean air without nuclei requires humidities of 420% before condensation will start. Negative ions (see p. 72) probably act as nuclei under these conditions.

In the finest haze the condensation droplets are usually 1 μ. After they have grown to 50–200 μ, so-called *cloud* or *drizzle particles* are formed. Before droplets start to precipitate *(rain particles)* the size should increase to above 200 μ. Two important processes have been suggested to explain this:

(1) The *ice-crystal process.* In clouds which for several reasons (lack of sublimation nuclei, etc.) are supercooled, ice crystals will grow rapidly at the expense of water droplets because of the lower vapour pressure of ice than of water.

(2) The *gravitational coalescence process.* In the tropics, where entire clouds may have temperatures above 0°C, droplets seem to increase in size, either through coalescence as they fall through the air, or through growth of cold drops at the expense of warm ones due to differences in vapour pressure.

Various types of precipitation are distinguished: *rain* (drops of 200–7000μ), *drizzle* (droplets of 50–500μ, floating on air currents), *sleet* (more or less spherical, hard pellets of ice), *hail* (round ice stones with concentric structures), *snow* (composed of hexagonal ice crystals), etc. The fall is usually accompanied by considerable disturbances of the electric field of the atmosphere (see p. 73).

Fog can be formed as a result of condensation at low level. Favourable conditions for fog formation are the colder seasons of the year with little turbulence and light winds. These conditions prevail in W. Europe under high atmospheric pressures (770–780 mm), particularly near the coast with ample supply of moisture. Many classifications have been suggested, the following being fairly simple and practical:

(1) *Air mass fog.* It is related to specific air masses. (*i*) *Advection fog,* due to warm moist air passing slowly over cool surfaces. This could happen in winter if warm air masses from the sea enter the colder continental area. The reverse takes place in summer when the sea is colder than the land. This is the cause of the notorious fog around New Foundland and Labrador in summer when warm continental air moves over cold sea water. Owing to convective cooling, fog known as *convective fog* is formed. (*ii*) *Radiation fog,* on account of local cooling of moist air above the ground consequent upon strong heat radiation loss of the soil (on clear nights for example). If the wind is quite calm, no fog will be formed. Slight air movement is still required, otherwise moisture of the lowermost air layer is only deposited on the ground as *dew.* (*iii*) *Steam fog,* due to addition of moisture of the air when cool air passes over a warm evaporating water surface (*e.g.* above lakes or rivers). (*iv*) *Up-slope fog,* due to air moving up a mountain slope and being cooled by expansion.

(2) *Frontal fog.* This type of fog often occurs in advance of a warm front overtaking a cold air mass, because warm rain from the frontal surface is falling through the cold air. The warm rain evaporates and saturates the cold air, causing fog. The same may occur behind slow moving cold fronts.

As fog greatly affects the respiration of man, in particular of people suffering from a decreased bronchial capacity, in biometeorological studies a sharp distinction should be made between the type of fog which is being studied. Also many air pollution and smog problems, to be discussed in Chapter 4 of this Part, are closely associated with the fog phenomenon. The study of these problems therefore requires a thorough knowledge of the mechanism of fog formation and of the physical properties of fog. In this connection it may also be said that along the sea coast of W. Europe fog will differ in its electrical properties, depending on the direction of the wind. A west wind usually carries much salt into the fog, which causes considerable insulation losses in electric recording equipment. The same fog with an east wind is usually harmless. This might be another reason why different biological effects of fog occur at different periods of the year.

In the previous pages we have described a number of important bioclimatological factors: temperature, humidity, atmospheric pressure, wind (speed and direction), and condensation and precipitation. Another very important factor is known as global sun and sky radiation. Prof. N. Robinson, Head of the Solar Physics Laboratory of the Israel Institute of Technology, Haifa, Israel, prepared this special section of the book.

Section 6. Global Solar and Sky Radiation and Their Main Spectral Regions

by

N. ROBINSON

1. Definition of Global Radiation (T), Solar Radiation (S) and Sky Radiation (D)

Part of the radiation emitted by the sun reaches the earth directly *(Solar radiation, S)* and part in the form of scattered radiation *(sky radiation, D)*; the latter radiation originates in the atmosphere as a result of scattering processes. The sum of the two kinds of radiation, incident on a horizontal plane, is called *global radiation (T)*. The interest of bioclimatology in the solar spectrum is usually confined to the wavelengths reaching the earth's surface in appreciable quantities and affecting the living organisms. At sea level under favourable atmospheric conditions the shortest wavelength is about 2900 Å and the longest about 30,000 Å (1Å = 0.1 mμ = 10^{-8} cm).

It is customary to divide the solar spectrum into three main regions: *the ultraviolet* (U.V.) (subdivided into part *A* and part *B*), the *visible*, and the *infrared* (I.R.). The amounts of energy of *T*, *S*, and *D* reaching the surface of the earth, as well as the energy distribution in their spectrum, depend on various cosmic and atmospheric conditions and the elevation above sea-level (*H*).

Four factors have to be taken into account:

(1) The *varying distance between the sun and earth.* This determines the intensity of energy reaching a given point on the earth's surface.

(2) The *sun's altitude* ($h_{\odot}$) or the *air mass** (m). These two quantities are connected by the expression

$$m = \frac{1}{\sin h_{\odot}}$$

(3) The *length of the day* which determines the daily sums of energy.

(4) The *cloudiness* which has its specific characteristics at every point and cannot be treated in a general manner. This factor must be based on statistical data over a considerable period of time and only mean values of sun radiation reaching the earth due to cloudiness can be computed.

Some examples of daily sums of T in its yearly course for different places are given in Figs. 3A[86], 3B[77] and 3C[91]. Figures 4A[86], 4B[92, 93] and 4C[91] will give

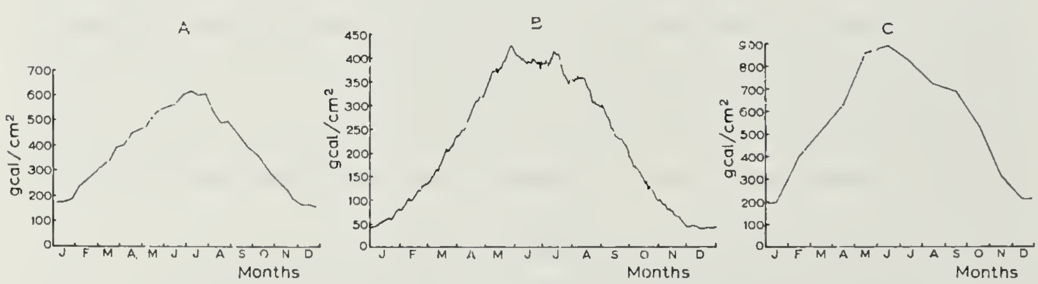

Fig. 3.
Yearly course of global radiation (T). A, for Missouri; B, for Belgium; C, for Haifa.

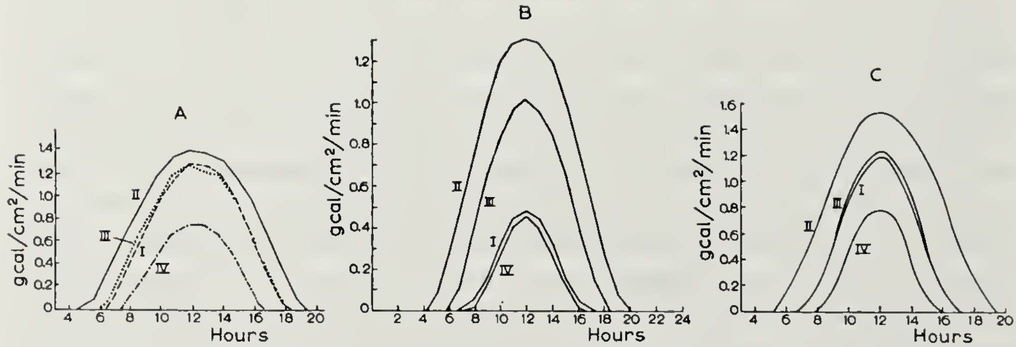

Fig. 4.
Daily course of global radiation (T). A, for Missouri; B, for Austria; C, for Haifa. Curve I for mid-March, curve II for mid-June, curve III for mid-September, curve IV for mid-December.

* This air mass concept is different from the concept described on p. 17.

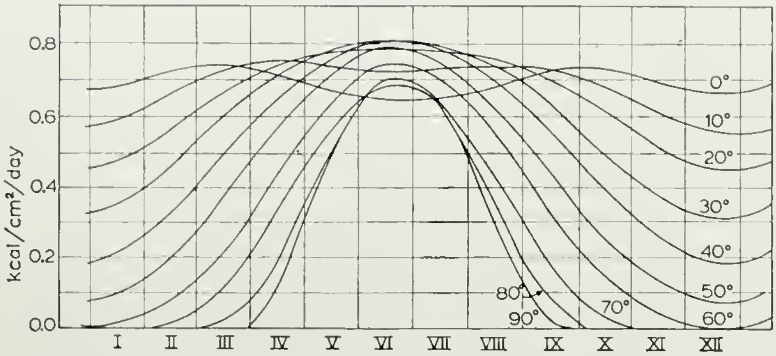

Fig. 5.
Yearly course of direct radiation (S) at different geographical latitudes.

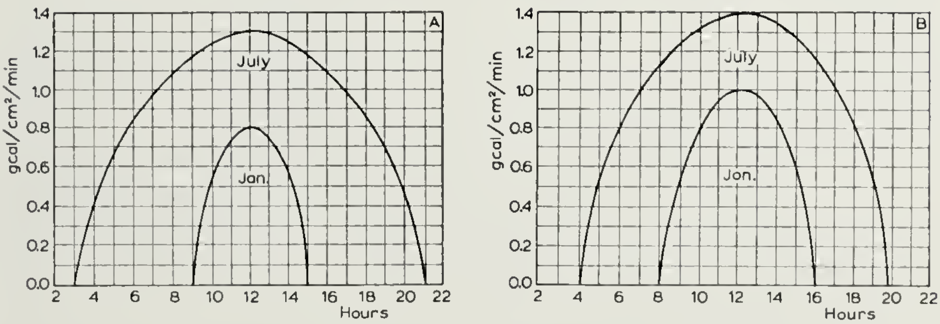

Fig. 6.
Daily course of direct radiation (S). A, for Pavlosk (U.S.S.R.); B, for Haifa.

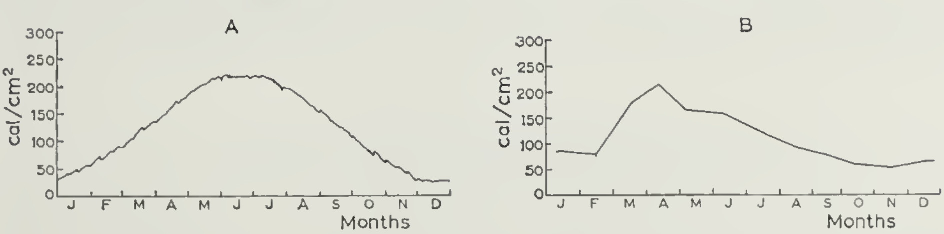

Fig. 7.
Yearly course of sky radiation (D). A, for Belgium; B, for Haifa.

examples of the daily course of T. The yearly course of the direct sun radiation S for different latitudes is given in Fig. 5[83]. The daily course of S is demonstrated in Figs. 6A[83] and 6B[91]. Examples of the yearly course of the sky radiation D for Belgium and Israel are given in Figs. 7A[77] and 7B[91]. Table 2 shows the combined dependence of the direct solar radiation S, incident on a horizontal surface, on $h_{\odot}$ and on H for the Eastern Alps, expressed in mcal/cm²/min.

TABLE 2

THE DEPENDENCE OF S ON $h_{\odot}$ (SUN'S ALTITUDE) AND H (ELEVATION ABOVE SEA LEVEL)

	$h_{\odot}$					
	10°	*20°*	*30°*	*40°*	*50°*	*60°*
H in mm						
200	0.104	0.311	0.531	0.744	0.930	1.082
500	0.118	0.337	0.565	0.782	0.965	1.117
1000	0.142	0.379	0.618	0.838	1.060	1.182
1500	0.165	0.415	0.665	0.890	1.078	1.241
2000	0.183	0.446	0.703	0.936	1.137	1.295
3000	0.199	0.474	0.742	0.987	1.193	1.370
Difference						
3000–200	0.095	0.163	0.211	0.243	0.263	0.288
Ratio						
3000:200	1.92	1.52	1.39	1.33	1.28	1.27

The increase of S with $h_{\odot}$ and H is due to two factors:

(1) The different pathlength of the sun's rays in the atmosphere (m).

(2) The difference in total thickness of the atmosphere. Both factors influence the quantity of aerosols encountered by the sun's rays. These aerosols diminish the solar radiation. Therefore, no proportionality between S and H is to be expected.

The data in Table 2 indicate that the absolute values of S for different H values increase more rapidly with increasing values of $h_{\odot}$ (see difference between H 3000 and 200 mm); on the other hand, the ratio between the S values for H = 3000 and H = 200 mm is greatest with small $h_{\odot}$.

TABLE 3

THE DEPENDENCE OF D ON $h_{\odot}$ AND H

	$h_{\odot}$					
	10°	*20°*	*30°*	*40°*	*50°*	*60°*
H in mm						
200	0.050	0.082	0.109	0.126	0.140	0.151
500	0.048	0.078	0.102	0.118	0.131	0.144
1000	0.046	0.072	0.091	0.105	0.117	0.126
1500	0.044	0.066	0.082	0.093	0.104	0.114
2000	0.042	0.062	0.075	0.084	0.094	0.103
3000	0.038	0.053	0.063	0.070	0.078	0.085
Difference						
3000–200	0.012	0.029	0.046	0.056	0.062	0.066
Ratio						
3000:200	0.76	0.65	0.58	0.56	0.56	0.56

The sky radiation D also depends on H and on $h_{\odot}$, because the scattering particles in the atmosphere change in number and in size distribution with $h_{\odot}$ and H; one example of this for the Eastern Alps is given in Table 3 for a clear sky in mcal/cm²/min.

2. *The Influence of Cloudiness on T, S, and D*

The influence of cloudiness on the amount of energy reaching the earth depends on the height, the kind, the thickness and the composition of clouds.

T is little reduced by scattered clouds, even if cloudiness reaches 50%, because of the strong reflection of radiation by them. This reflection compensates for the energy lost by absorption in the clouds.

A summary of reflection, transmission and absorption of S as a function of cloud thickness is given in Fig. 8 (ref. [83]), the influence of cloudiness on D is expressed in Fig. 9.

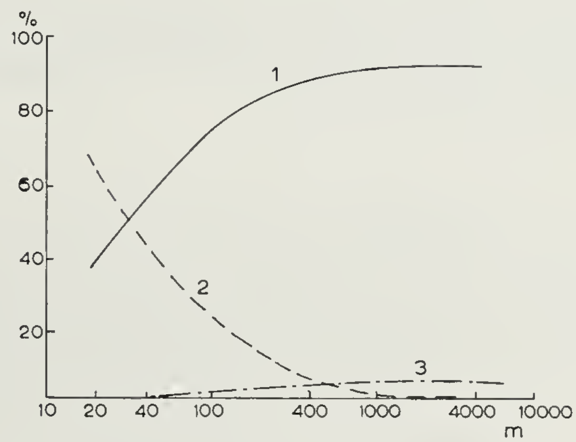

Fig. 8.
Influence of clouds on direct radiation (S). 1, for reflection; 2, for penetration; 3, for absorption.

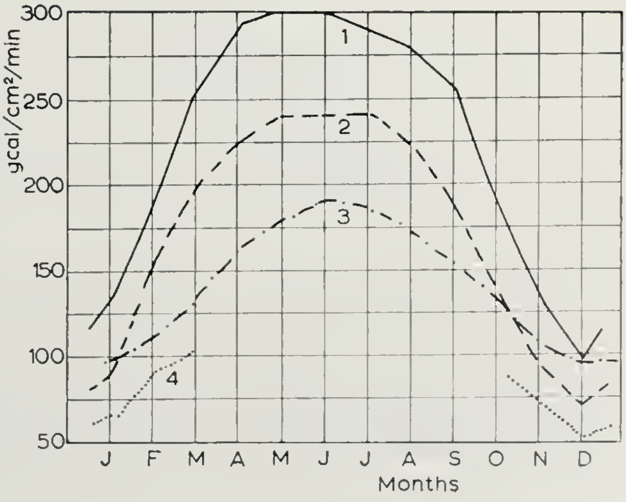

Fig. 9.
Influence of cloudiness on sky radiation (D). 1, for high and medium clouds; 2, for low clouds; 3, for cloudless sky; 4, for fog.

3. *The Spectra of T, S and D*

The energy distributions in the spectra are functions of m (or $h_{\odot}$), of H and of the state of the atmosphere.

The atmosphere affects the radiation passing from the sun to the earth by scattering, absorption and reflection.

Scattering is a selective phenomenon. The scattering by pure air is proportional to λ^{-4}. Hence, for example, the radiation of wavelength $\lambda = 3800$ Å will be scattered 16 times more than that of $\lambda = 7600$ Å. Absorption is likewise selective.

A "turbidity factor" was introduced by Linke as a general and comprehensive characteristic of the influence of the atmosphere on radiation. This factor is equal to the number of ideal atmospheres which would cause the same diminution of the sun's radiation as that caused by the actual atmosphere. This factor must be defined for every wavelength separately. The combined influence of m and H on the energy distribution in the S spectrum is shown in Fig. 10 (ref. [78]).

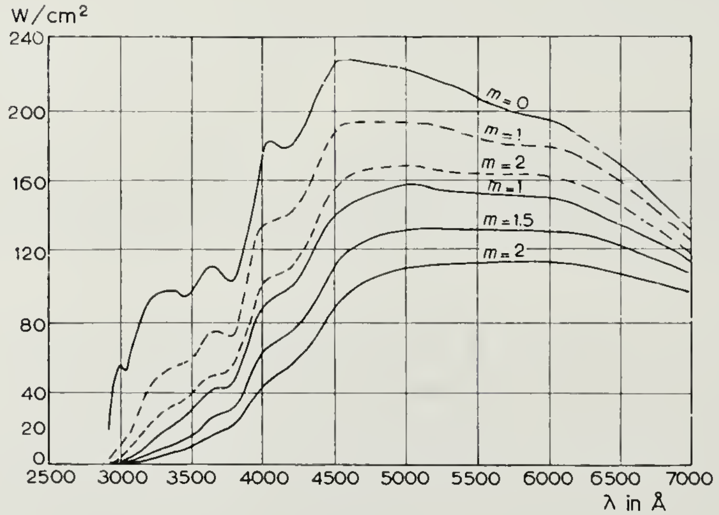

Fig. 10.
Influence of air mass (m) and elevation above sea level (H) on the energy distribution in the solar spectrum. Dotted lines, for H = 1789 m; drawn lines, for H = 0 m; W = Watt.

The energy distribution of the D spectrum has features different from those of S. An example of this kind of an energy distribution for different points in the sky is given in Fig. 11.

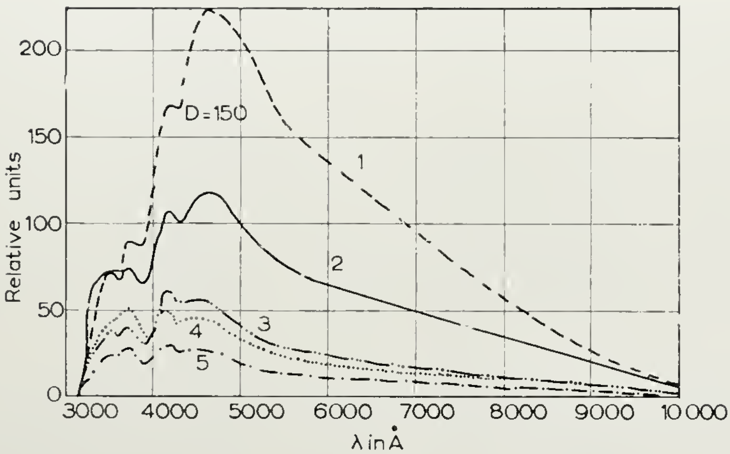

Fig. 11.
Energy distribution in the spectrum of sky radiation for different points of the sky. Curve 1, for 150° from the sun; 2, for 10°; 3, for 120°; 4, for 45°; 5, for 75°.

4. *The Total U.V.: 3800 Å ≧ λ ≧ 2900 Å*

This spectral region is very important for biometeorological phenomena (actually out of proportion to the radiation intensity) in spite of the fact that it contains only a small fraction of total solar energy reaching the earth. In Table IV the intensities of this radiation, as a percentage of the total energy reaching the earth, are given as a function of m (for S-U.V.).

TABLE 4

THE INTENSITY OF THE U.V. AS COMPARED WITH THE TOTAL RADIATION ENERGY AT DIFFERENT VALUES OF m $\left(= \frac{1}{\sin h_{\odot}}\right)$

m	0	0.5	1	2	3	4	6	8	10
U.V. in % of total energy	6.7	5.3	4.2	2.7	1.8	1.1	0.5	0.2	0.1

In absolute units the energy of the total U.V. for $\lambda < 3500$ Å as a function of $h_{\odot}$ is given in Fig. 12 (ref.[81]). As mentioned before, this part of the spectrum is of exceptional interest to biometeorology. Table 5 gives a summary of a few important biological effects of U.V. radiation. All these effects vary considerably with λ, as shown in Fig. 13 (ref.[88]).

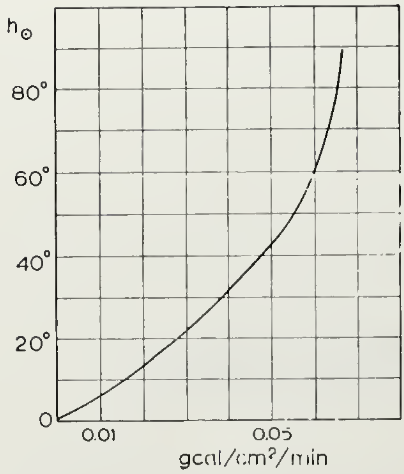

Fig. 12.
The change of U.V. intensity with sun's altitude (h⊙).

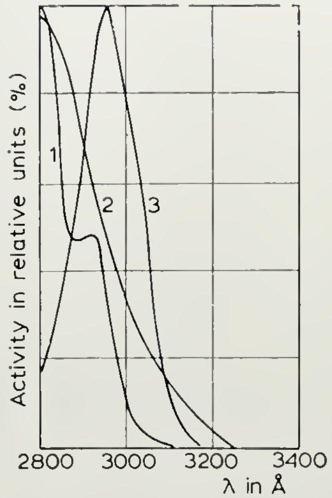

Fig. 13.
Different biological effects of U.V. radiation. 1, on vitamin D formation; 2, on hampering growth of tissues; 3, on erythema.

TABLE 5

THE BIOLOGICAL EFFECTS OF U.V. RADIATION

1. Bactericidal effect till	3050 Å
2. Creation of (antirachitic) vitamin D till	3100 Å
3. Erythema till	3150 Å
4. Albumen coagulation till	3250 Å

It should be stressed that only the absorbed radiation has an effect according to the Grotius-Draper law. Without knowing the degree of absorption by an object, nothing can be said about the effects of U.V. radiation. It is known that in this spectral region organic compounds absorb rather considerably and the biological effects of this radiation are therefore noteworthy.

As U.V. is strongly scattered by the atmosphere (the scattering by the air being proportional to λ^{-4}) and both the direct and the scattered radiation show high values, they will be dealt with separately.

The direct U.V.-solar radiation (S-U.V.)

An example of the total amount of this radiation and the energy distribution in its spectrum is given in Fig. 10. From these curves may be seen that the energy decreases with increasing m, that the curves have a steep slope towards short λ and that the lowest value of λ—λ_m increases with m. Besides

m, an important factor influencing the U.V. is H as shown in the same figure. From these curves it is evident that the energy of U.V. radiation increases considerably with H.

One fact of particular importance to biometeorology should be pointed out: although the quantity of total U.V. radiation and the energy distribution in its spectrum are very sensitive to H, the λ_m is almost independent of H, as may be seen in Table 6[81]. This can be explained by the fact that the lowest limit for U.V. radiation is defined rather by the O_3 layer in the upper atmosphere than by the influence of the troposphere.

TABLE 6

THE SHORTEST U.V. WAVELENGTH AT DIFFERENT VALUES OF H

H in meters	50	116	1620	3136	4560
λ in Å	2912.6	2912.4	2913.6	2911.0	2912.1

The scattered U.V.-sky radiation (D-U.V.)

The D-U.V. is a very important part of the total U.V. Firstly it contains a large part of the total U.V. due to pronounced scattering by the atmosphere, secondly, being undirected, the D-U.V. surrounds the irradiated object from all sides and is found in measurable quantities in the optical shadow of various objects: houses, trees, etc. Thus *appreciable doses of U.V. can be received without direct exposure to the sun.* Fig. 14 shows the D-U.V. penetrating into the optical shadow of an object[90]. The spectral curves for the D-U.V.

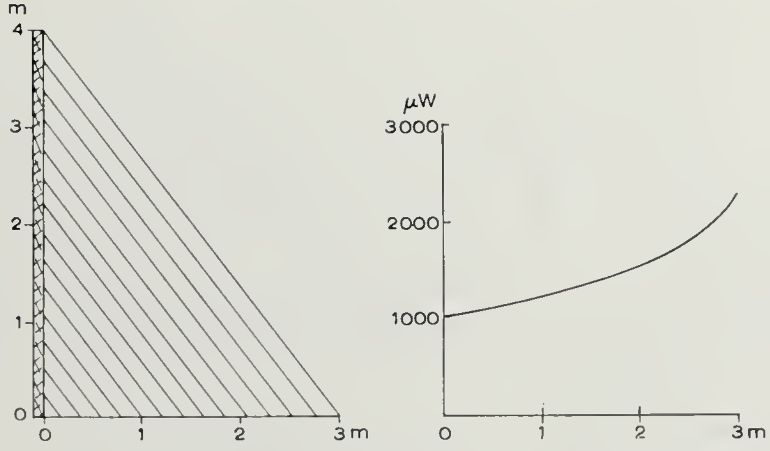

Fig. 14.
Penetration of scattered U.V. radiation into the optical shadow of an object.

are different from those for *S*-U.V., as seen in the curves in Fig. 11. For these curves the energy of $\lambda = 5000$ Å was taken as a unit.

Ultra violet A and B

The ultraviolet spectrum can be divided into 2 parts: *ultraviolet A* and *B*.

Ultraviolet A: 3800 Å $\geqq \lambda \geqq$ 3150 Å

This part of the U.V. radiation contains approximately 90% of the total U.V. reaching the earth. Yet, its effect upon living organisms having been underestimated until recently, it has not received the earnest study it deserves.

Proteins and nucleonic acids are known to absorb radiation to some extent up to $\lambda = 4000$ Å. It was found, moreover, that the U.V.-*A* causes an immediate erythema due to U.V. with $\lambda > 3200$ Å, which seems to be the result of the penetration of these wavelengths as far down as the peripheral blood arterioles. In this connection the spectral transparency of the different layers of the human skin is shown in Fig. 15 for the U.V. range[68] (for further details see p. 339).

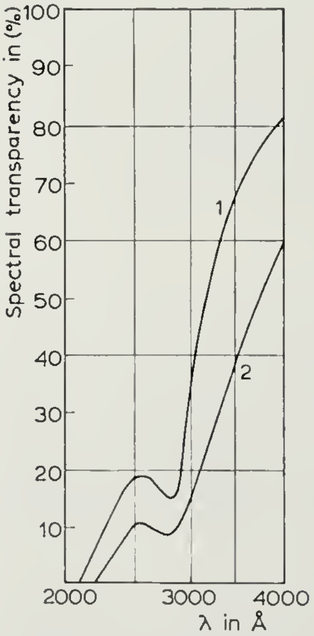

Fig. 15.
Spectral transparency of the human skin. Curve 1, for horny layer; curve 2, for epidermis.

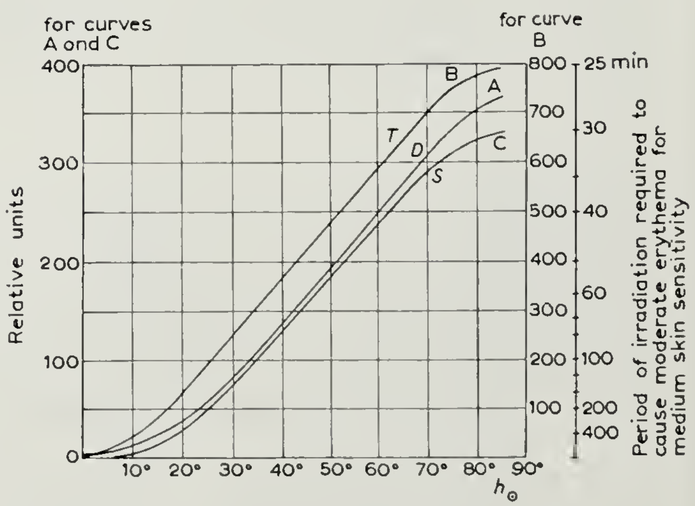

Fig. 16.
Ultraviolet-*B* radiation for clear sky depending on altitude of sun $h_\odot$.

The dependence of U.V.-*A* on *m* is not very appreciable: it changes in Central Europe at sea level in the ratio of 5:1 from noon to the maximum of *m*.

Ultraviolet B: 3150 Å $\geqq \lambda \geqq$ 2900 Å

The most important part of the U.V. in the lower atmosphere is the U.V.-*B*. Its total energy and spectral distribution depend very much on *m* and *H*.

The *dependence on* $h_\odot$ of U.V.-*B* in Davos-Units is shown in Fig. 16[69]. Curve A represents the U.V.-*B* radiation for *D* on a horizontal plane; curve C for *S* on a plane perpendicular to the sun's rays; curve B for *T* on a horizontal plane. The X-axis is $h_\odot$, the Y-axis is divided into two scales, one (left) applying to curves A and C, the second (right) to curve B. The time necessary for a moderate erythema is given in addition to the Davos Units on the Y-axis. These curves may be used with caution for different places, using $h_\odot$ as variable.

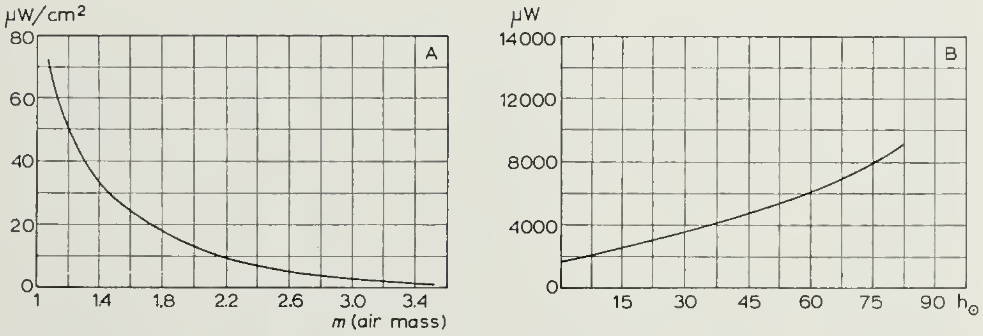

Fig. 17.
Change of U.V. with altitude $h_\odot$. A, for Washington, D.C.; B, for Haifa.

In Figs. 17A[72] and 17B[90] the dependence of the U.V.-*B* on $h_\odot$ is given in absolute units for Washington D.C. and for Haifa respectively. This figure shows clearly how rapidly the energy of U.V.-*B* decreases with *m*.

The daily course throughout the year for low-lying land in Davos-Units on a horizontal plane for *T*-U.V.-*B*, *D*-U.V.-*B* and *S*-U.V.-*B* is given in Table 7[69]. This table shows that *D is more intense than S*. At noon in December the ratio is 4:1 and in June about 1.4:1. If the sun's altitude is low, *e.g.* in the morning (at 8 a.m.) and afternoon (at 4 p.m.), these ratios correspond to 4:1 and 2.3:1.

The *total intensity of all three components (T, S, D) is greater in summer than in winter;* at noon for *S* the ratio of summer to winter is almost 17:1, for *D* it is 5.5:1 and for *T* about 8:1. From the data in Table 7 the daily sums of all three components have been computed and presented in Table 8.

TABLE 7

DAILY COURSE OF *S*-U.V.-*B*, *D*-U.V.-*B* AND *T*-U.V.-*B*

Hours	5 19	6 18	7 17	8 16	9 15	10 14	11 13	12	
January	—	—	—	3	9	11	15	18	
February	—	—	4	7	13	27	34	37	
March	—	—	7	13	30	58	82	90	
April	—	5	11	33	73	115	147	163	
May	3	9	24	57	109	162	200	210	
June	4	10	32	71	120	186	224	240	*S*
July	4	10	29	67	123	178	215	237	
August	—	8	17	41	87	138	172	185	
September	—	2	8	19	45	78	109	128	
October	—	—	2	8	17	35	47	56	
November	—	—	—	3	9	14	20	23	
December	—	—	—	1	7	9	12	14	
January	—	—	—	5	24	45	66	72	
February	—	—	2	20	52	83	106	72	
March	—	—	18	55	100	147	173	185	
April	—	15	50	105	165	210	243	257	
May	9	36	88	147	204	258	298	310	
June	15	50	103	164	220	279	316	330	*D*
July	14	45	99	163	217	270	313	323	
August	2	23	68	124	183	232	268	280	
September	—	—	30	76	125	172	211	228	
October	—	4	7	32	71	108	134	147	
November	—	—	—	11	31	57	79	89	
December	—	—	—	4	18	37	53	60	
January	—	—	—	8	33	56	81	90	
February	—	—	6	27	65	110	140	165	
March	—	—	25	68	130	205	255	275	
April	—	20	61	138	238	325	390	420	
May	12	45	112	204	313	420	498	520	
June	19	60	135	235	350	465	540	570	*T*
July	18	55	128	230	340	448	528	560	
August	2	31	85	165	270	370	440	462	
September	—	6	38	95	170	250	320	356	
October	—	—	9	40	88	143	181	203	
November	—	—	—	14	40	71	99	112	
December	—	—	—	5	25	46	65	74	

It should be realized that the total energy irradiated per day for *D* is 9.3 times greater in June than in December, 23.5 times for *S* and 12 times for *T*.

U.V.-B depends not only on $h_{\odot}$ *but also on H.* This is presented for *T* in Table 9[92] and for *S* in Table 10[92], for both cases on a horizontal plane in relative units. From these data it is clear that the influence of *H* is greater in winter than in summer. Therefore *in winter the intensity of radiation in-*

TABLE 8

DAILY SUMS OF U.V.-B (S, D AND T)

Months	S	D	T
January	1.022	3.536	4.558
February	2.306	6.310	8.616
March	4.592	11.798	16.390
April	9.523	14.946	27.570
May	13.713	23.782	37.495
June	15.456	26.196	41.650
July	15.006	25.434	40.440
August	11.288	20.582	31.870
September	7.336	14.184	21.520
October	2.912	8.298	11.210
November	1.274	4.384	5.658
December	0.662	2.824	3.486

TABLE 9

THE DEPENDENCE OF T-U.V.-B ON H

H in m	200	500	1000	1500	2000	3000
Summer %	100	110	118	125	130	134
Winter %	100	112	126	140	150	172

TABLE 10

THE DEPENDENCE OF S-U.V.-B ON H

H in m	200	500	1000	1500	2000	2500	3000	3500
Summer %	100	125	145	170	182	190	195	200
Winter %	100	150	220	280	330	390	440	480

TABLE 11

THE SEASONAL INFLUENCE OF H ON U.V.-B

for S	for D	for T
1720%	550%	770%

creases more rapidly with H than in summer. A comparison of the data of Tables 9 and 10, shows that T is *less sensitive* to H than S. This may be explained by the fact that the D-U.V.-B is almost constant to H = 3300 m.

The influence of summer and winter on the values of U.V.-B during a cloudless day at sea level is given in Table 11[92]. The figures indicate the percentages of the summer values of S, D and T as compared with the winter values.

The combined influence of $h_{\odot}$ and H on U.V.-B for 2800 Å $\leq \lambda \leq$ 3100 Å in the Crimea, in relative units, is demonstrated by the data in Table 12[64].

TABLE 12

THE COMBINED INFLUENCE OF $h_{\odot}$ AND H ON U.V.-B

H	*Time of observation*	*Sun's altitude in degrees*										
		15	*20*	*25*	*30*	*35*	*40*	*45*	*50*	*55*	*60*	*65*
1180	a.m.	5.0	7.3	15.0	20.0	45.0	82	127	245	350	450	576
	p.m.	4.8	5.4	14.2	24.0	35.0	55	90	130	217	360	492
701	a.m.	—	5.0	13.0	15.0	33.0	35	89	170	255	330	466
	p.m.	—	—	11.0	17.0	28.0	40	75	105	175	250	360
470	a.m.	3.5	4.2	8.0	12.0	23.0	45	57	113	190	270	440
	p.m.	—	—	—	11.0	18.0	32	45	85	130	250	342
120	a.m.	1.8	3.6	5.0	7.0	15.0	28	40	85	143	242	280
	p.m.	1.8	3.8	4.6	6.0	12.0	15	28	54	85	128	242
0	a.m.	—	3.9	4.5	6.0	10.0	22	32	72	90	233	250
	p.m.	—	2.5	4.0	4.9	7.2	12	25	38	70	100	190

In general U.V.-B radiation is stronger before than after noon for the same value of $h_{\odot}$. The influence of $h_{\odot}$ is very potent: an increase of $h_{\odot}$ from 15–65° causes an increase of this radiation by a factor of 100.

Owing to the strong scattering of U.V.-B in the atmosphere, the quantity of U.V.-B depends on the orientation of the irradiated object. A comparison of the irradiated quantities of U.V.-B on a horizontal plane and on a vertical one, per unit of area, is of importance for biological and biometeorological purposes. Such a comparison, in relative units for all three components of U.V.-B (S, D and T) for a clear sky is presented in Table XIII[92].

TABLE 13

U.V.-B INTENSITY ON A HORIZONTAL AND ON A VERTICAL PLANE

	March			*July*			*October*			*December*		
	S	D	T	S	D	T	S	D	T	S	D	T
Horiz. plane	25	50	75	133	132	265	43	89	132	2	14	15
Vert. plane	36	84	119	96	199	295	62	151	213	5	23	28

For large $h_{\odot}$ the horizontal plane receives more S than a vertical one. For small $h_{\odot}$ the opposite is true. All the year round the D-U.V.-B is more intense on a vertical than on a horizontal plane, because of the strong undirected radiation due to scattering. T is also more intense on a vertical than on a horizontal plane; the differences are usually larger than for D (except in summer with differences of $T < D$).

Frequently the ratio (r) between T-U.V.-B incident on a horizontal plane and on a surface perpendicular to the sun's rays is taken into consideration. This ratio is almost independent of $h_{\odot}$, except for small values of $h_{\odot}$, but depends appreciably on H, as shown in Table 14. The figures in this table represent the ratios for $h_{\odot}$ between 30° and 50°; for $h_{\odot}$ = 60° the values have to be increased by approx. 0.2.

TABLE 14

RATIO BETWEEN T-U.V.-B ON A HORIZONTAL PLANE AND ON A PLANE PERPENDICULAR TO THE SUN'S RAYS

H in mm	0	500	1000	2000	3000
r	2.0	1.7	1.6	1.5	1.3

For *heliotherapy* (see later p. 616) the irradiated *dose* is of importance. The dose is defined as the product of intensity of the radiation and the time of exposure. An example of such a dose for Davos, Switzerland, is demonstrated in Fig. 18, the curves A, B for a horizontal surface, the curves C, D for a plane perpendicular to the sun's rays.

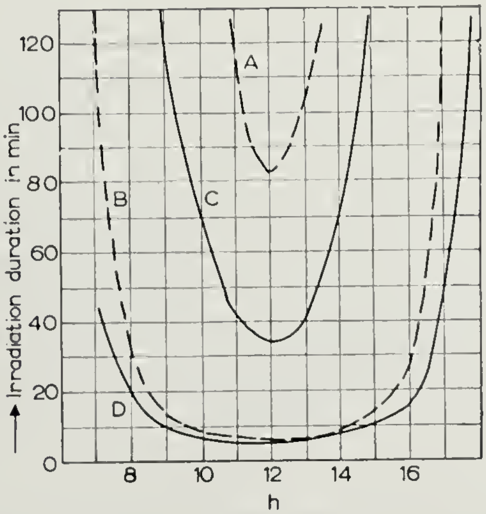

Fig. 18.
Doses of radiation. A and B, on a horizontal plane; C and D, on a plane perpendicular to the sun's rays.

5. *The Visible Part of the Sun's Spectrum: 3850 Å ≦ λ ≦ 7800 Å*

This part of the spectrum is called "visible" as its wavelength (λ) limits coincide with those of the vision of a normal human eye.

It is necessary to distinguish between the total visible part of the solar spectrum and a part of it as perceived by the human eye, which is called light. Because of the two kinds of receptors of the human eye*, the spectral curves of vision are differerent (Fig. 19: the curve A for high brightness and the curve B for low brightness; C is the total visible part of the sun's spectrum). It is clear that in weak light, such as moonlight, the objects appear "bluer". This phenomenon is known as the *Purkinje effect*.

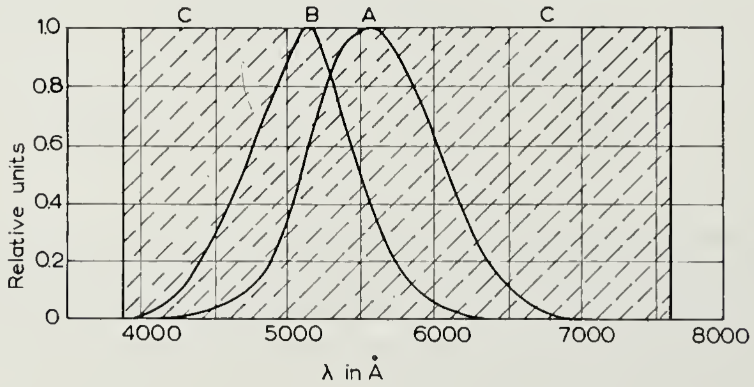

Fig. 19.
Luminosity curves. A, for high brightness; B, for very low brightness; C, total visible.

The total amount of the energy in the visible part of the spectrum and the energy distribution in its spectrum depend on *m*, *H* and on the state of the atmosphere (see Fig. 10).

If for all wavelengths, within the visible part of the sun's spectrum, the energy of radiation is changed at the same ratio it affects only the intensity of light. However, a change in energy in different proportions for the different wavelengths causes also a change in the colour of light.

6. *The Infrared Part: 7800 Å ≦ λ ≦ 30,000 Å*

From the point of view of quantity of energy, this part of the spectrum contains about 50% of the total energy reaching the earth. Its biological

* Note by S.W. Tromp. The retina of the eye contains two types of cells, the rods and cones. The rods are mainly concerned with perception of light of low intensity; the cones are used for acute vision in bright light and colour perception. Whereas many rodcells may be connected to one nerve cell and fibre, each cone is often connected to a single nerve cell. Therefore rods transmit a light stimulus in a rather fuzzy way, whereas each cone sends usually a separate message to the cortex of the brain.

effect is the opposite of that of U.V., *i.e.* less in quality and more in quantity.

The total amount of I.R. changes with m; from $m=0$ to $m=10$ the I.R. increases by a factor of 1.5. Not only does the absolute value of I.R. decrease with increasing $h_{\odot}$, but also the ratio between this energy and the total sun energy reaching the earth. For $h_{\odot} = 2°$ this ratio is 0.8 and is only 0.5 for $h_{\odot} = 50°$. The I.R. is strongly absorbed by water vapour in the atmospher, hence the I.R. will be more intense in dry areas and on days of low humidity. This is also the reason why, with increasing H, the amount of I.R. also increases.

The amount of D-I.R. depends not only on $h_{\odot}$ (m), but also on the aerosol content of the atmosphere, the quantity and size of the particles and their distribution. Generally the I.R. is called *heat radiation*. From the biological point of view this part of the spectrum is interesting, as this radiation penetrates deepest into the living tissue. For further details we may refer to Part IV, p. 345.

Section 7. Electric Properties of the Atmosphere

The electric and electromagnetic properties of the atmosphere show up at least in four different ways: ionization, electric conductivity, potential gradient and electromagnetic long waves (wave length 6–100 km).

Subsect. A. IONIZATION AND ELECTRIC CONDUCTIVITY

The atmosphere contains a large number of charged particles, ions, which are often classified into two groups: small ions and Langevin ions.

Small ions

They are composed of electrically charged clusters of molecules of atmospheric gases, with great mobility (1 cm/sec in an electric field of 1 V/cm) and an electric charge per ion of $15.9 \cdot 10^{-20}$ coulomb. On the average there are 500–600 small ions of each sign in 1 cm^3 of air (number of ordinary molecules in 1 cm^3 dry air at 0°C and 76 cm pressure $= 2.75 \cdot 10^{19}$).

Langevin ions

These are sluggish ions with charges attached to *Aitken nuclei,* the hygroscopic particles on which moisture condenses when clouds are formed. They are considerably less mobile (average velocity 0.0005 cm/sec) than the smal ions. In places where the atmosphere is polluted by dust and products of combustion of coal, Aitken nuclei are more frequent than small ions. Values of 50,000 and more Langevin ions/cm^3 are common near towns. The atmosphere contains positive and negative ions, but the observation that in general the potential gradient (see further) falls off as we ascend in the atmosphere (indicating that the net charge of the air is positive) suggests that there must be an excess of positive ions.

As a result of the presence of ions, the air has a certain electric *conductivity*. Variations in conductivity are usually explained by the different proportions of large and small ions, differences in speed and presence of conductors.

(1) If large ions are formed (*e.g.*, in strongly polluted atmosphere) at the expense of small ions, the effective conductivity is reduced because of the smaller mobility of the Langevin ions and the air-earth current (see further) is maintained by a higher potential gradient.

(2) The general mobility of negative ions is usually greater than that of positive ions. A ratio of 1:100 has been found in certain gases.

(3) The ratio between both velocities decreases in humid air (in dry air about 1.54, in humid air 1.09); it increases with decreasing atmospheric pressure (according to Townsend in 1899) and increases with rising temperature (according to McClelland).

(4) According to Leiri (in 1934), ionizing sources (*e.g.*, an electric tension of 190 V/cm)often create 57 times more negative than positive ions.

(5) Küster and Janitzky (in 1932) were able to demonstrate the influence of metal conductors: (*i*) Air brushing past a metal surface through a pipe is positively charged: (*ii*) The surplus in positive ions increases if the metal surface is heated; (*iii*) The surplus decreases if the metal surface is lacquered.

As a result, in the neighbourhood of an iron stove or central heating pipes, the air is rich in positive ions according to studies by Tchyevsky (in 1934). Air passing through insulated pipes absorbs up to 30% of the ions of the air.

Since free ions of opposite sign tend to re-combine and give up their charges, there must be active causes of ionization at work (see further). The rate of re-combining is greatly influenced by the different factors, mentioned above, which affect the velocity of ionic movements.

The total effect of these various processes, determines the final conductivity of the atmosphere, which also varies as a result of different cosmic and meteorological influences. The deeper causes of all these factors are only partly known. Variations in ionizing power of cosmic sources are probably due to fluctuations in *cosmic radiation, ultraviolet solar radiation* (at high altitudes in the atmosphere ultraviolet waves with wavelengths less than 0.2μ seem to be important as an ionizing source) and *radioactive radiation* in the atmosphere (mainly due to radioactive emanations from the surface of the earth).

Other secondary sources of ionization are: electric charges created during *dust storms* in desert regions as a result of friction of mineral fragments; friction electricity between ice crystals in snow, known as *Rudge effect* (in whirling snow the electrostatic charges, either positive or negative, are usually of the order of $20 \cdot 10^{-9}$ coulomb/cm³, although values up to $205 \cdot 10^{-9}$ have been reported from single snow-flakes); electric charges due to the *breaking up of large falling water drops,* known as *Lenard waterfall effect.* This process is characterized by the formation of a number of small positively charged droplets, the corresponding negative charges being carried away by the finer spray of a waterfall or fountain or by air currents. Floating water drops of 2.5 mm diameter can be disintegrated by air currents of 20 m/sec, drops of 5.5 mm require currents of 10.9 m/sec. Such processes seem to be common, especially in thunderclouds with powerful ascending air currents. Although both positive and negative raindrops occur, the positive ones predominate. The charge per cm³ rain is generally less than $\frac{1}{3} \cdot 10^{-9}$ coulomb, although in a few cases charges of up to $20 \cdot 10^{-9}$ coulomb have been observed.

Differences have been noted between *land rain* and *thunderstorm rain.* During land rain 75% of the rain is usually positive: the potential gradient (see below) is often negative. Positive rain also usually dominates during thunderstorms. However, the electric charge per gram of rain is considerably larger than in the case of land rain. The potential gradients (see below) usually fluctuate between high positive and negative values, the latter dominating.

It has been found that on meteorologically undisturbed days inland the electrical conductivity reaches a maximum value during the night and minimum values during the day. This seems to be mainly due to the diurnal cycle of turbulence in the atmosphere, which changes the radioactive content of the air near the surface and transports contaminated air from the ground to higher altitudes in the atmosphere.

As indicated above, apart from these regular daily variations, the conductivity may change rapidly due to weather changes or changes in the amount of contamination of the air, *e.g.* near industrial centres. The conductivity of the air also changes with the level. Wigand demonstrated that 3 km up the conductivity increased to 5 times, 6 km up to 10 times and 9 km up to 26 times the ground value. According to Gish and Sherman the increase 18 km up is 100 times the ground value. This increment is partly due to increased ionization, but it is mainly caused by the greater mobility of the ions (because of decreased atmospheric density). At a height of 70–100 km, very high values were observed.

The conductivity of the air is usually recorded with a *Gerdien tube* (about 1 m long and 10 cm wide) through which air moves at a certain velocity. The ion currents to the inner collectors are measured with electronic electrometers capable of measuring currents as low as 10^{-16} A. The electrometer output is automatically recorded.

The ionization of the air is recorded in a similar way. A fixed amount of air is sucked through a tube with a metal needle in the centre or along a number of parallel insulated plates which are either positively or negatively charged with a battery. As a result, negative or positive ions are collected on those charged plates. The electric current created by the charges of the collected ions are recorded by very sensitive micro-micro-ammeters. In view of the very small currents involved the slightest loss of insulation disturbs the recording and it is because of this drawback that considerable reserve is advised towards many of the published data on ionization of the air. Further details concerning this extremely complicated problem are discussed in Part IV, Chapter 1 (pp. 351–369) by Krueger, Hicks and Beckett.

Subsect. B. POTENTIAL GRADIENT

Franklin discovered that a wire attached to a kite flying at a considerable height, even in fine weather, becomes electrified and sparks may be drawn from the wire. This proves that there is a large difference of potential between the ground and the air at the level of the kite. It is found that in the open the potential changes fairly uniformly with height. This rate of change is called the *potential gradient* of the atmosphere. In fine weather near the ground it is of the order of 120–150 V/m, the higher potential being at the greater height; the potential gradient is called positive in this case. Rising up from the earth, the potential continues to mount and at the levels attained by aircraft it may reach hundreds of thousands of volts. The potential gradient, however, diminishes as we go upwards. At 9 km height it is only a few V/m. The potential gradient fluctuates continuously, both in a horizontal and vertical direction. The different causes of the variations will be discussed presently.

1. Earth Charge

The existence of a positive potential gradient indicates the presence of a negative charge on the ground (known as earth charge) which is compensated by the positive charge of a layer of air approx. 9 km up. With a gradient of 100 V/m prevailing over the whole globe, the total charge of the earth would be $4.5 \cdot 10^5$ coulombs, *i.e.*, $9 \cdot 10^{-14}$ C/cm². This total charge of the earth is very small and can supply a current of only 1A for five days. As the gradient varies considerably and large areas might also have negative gradients, the value $4.5 \cdot 10^5$ C is only a very rough approximation. All in all, the earth with the atmosphere can be considered as a *spherical condenser* composed of a relatively well-conducting, negatively charged earth crust, a poorly-conducting, positively charged air layer of 80–100 km thickness and a very well-conducting ionosphere.

2. *Air-Earth Current*

The electric field of the atmosphere and the negatively charged earth crust together create an air-earth current, which continuously neutralizes the negative earth charge with the positive charge of the atmosphere. This current can be measured by substituting a metal plate for part of the ground. This current is roughly $8 \cdot 10^{-7}$ A/cm²/sec (according to other estimates $2 \cdot 10^{-6}$ A/km²), giving a total current towards the whole earth of 1400 A. Small as this current is, it suffices to neutralize the fine-weather charge on the ground in a fraction of an hour. During certain periods a negative potential gradient and, therefore, a reverse current can be observed. Rain, snow and lightning might also bring negative charges to the ground, but this alone can hardly explain the preservation of electric balance.

3. *Causes of Preservation of Balance between Positive and Negative Flow*

Various theories have been put forward to explain this extraordinary phenomenon, but so far none have succeeded in giving a completely satisfactory explanation. Only two of these theories will be briefly discussed.

(1) The *reverse current theory of C. T. R. Wilson* (1925). Measurements by G. C. Simpson and F. J. Scrase (in 1927) with an alti-electrograph demonstrated that the upper part of cumulo-nimbus clouds (*i.e.* heavy masses of clouds, with great vertical development, the summit of which rises as mountains or towers) practically always has a positive charge, the base being negative. This is explained by Simpson (in 1909) as being caused by the vigorous upward currents in cumulo-nimbus clouds, which break up the large raindrops and create droplets with positive charge. These accumulate at the upper end of the cloud. The smaller negative droplets escape sidewards and accumulate at the base of the cloud. According to Wilson, the negative base of these nimbus clouds induces a positive charge on the surface

of the earth which, as a direct result, repulses the positive ions of the atmosphere.

(2) The *electron-current theory of E. v. Schweidler* (1918) *and W. G. F. Swann* (1917). Schweidler and Swann assumed that a stream of electrons reaches the surface of the earth either as a corpuscular radiation from the sun or as a secondary radiation created by cosmic rays. Supporters of this theory pointed to the relation between northern lights phenomena and fluctuations of the potential gradient.

4. Causes of Variations of the Electric Field of the Atmosphere

The variations of the electric field of the atmosphere show up clearly in the fluctuations of the potential gradient, which normally has a positive value everywhere on earth. The principal causes of these variations are the following:

Influence of the topography of the earth's surface

In the neighbourhood of houses, trees, etc. lines connecting points of equal potential gradient in the air will rise upwards and fall again behind the obstacles. Only at a considerable height above the house the lines will be more or less parallel to the earth's surface.

Influence of weather conditions

The potential gradients depend to a great extent on the meteorological conditions of the atmosphere. During quiet weather conditions the gradient is usually low, higher when there is haze and it can be very high when certain types of fog prevail (values of 2,000 V/m have been recorded); during land-rain the gradient is mostly negative; throughout thunderstorms it fluctuates enormously between high positive and negative values, the latter being dominant (values of 10,000 V/m have been recorded); during snow-fall, high postitive and negative potential gradients occur; the potential gradient above the sea is usually low (115–140 V/m); near cities or industrial centres it can be high.

Influence of irregular distribution of the equipotential lines at the surface of the earth

Due to electro-chemical processes in the soil and artificial electric currents flowing through the earth's surface, electric fields are created in the earth's crust which show up at the surface as lines of equal earth potential affecting the potential gradient of the atmosphere.

Cosmic influences

(1) *Daily fluctuations.* The potential gradient shows a diurnal variation similar to the daily variation of the magnetic field. As the influence of weather on the fluctuations of the potential gradient usually dominates in northern latitudes, it is only clearly observed in equatorial regions. Mauchly discovered in 1926 that over the ocean and in polar regions the diurnal variations of potential gradient are governed by world-time, the minimum (107 V/m) occurring at 4 h Gr. M. T., the maximum (150 V/m) at 17 h Gr. M. T., the average gradient being greatest from October–March, smallest from April–September. According to Simpson the time of the maximal gradient (at 17 h Gr. M. T.) is the moment that the sun passes the meridian of the magnetic north pole. Studies at a great number of continental stations indicated fluctuations of the average daily amplitude of the potential gradient on land, either a simple oscillation or a double oscillation.

(2) *Yearly fluctuations.* An average of 20 stations on land indicated fluctuations of the average yearly amplitude of 20 to 239 V/m. Stations north of 30°N and south of 40°S show a pronounced yearly oscillation of the daily fluctuations with a maximum between November and January and a slight minimum between July and August; of the stations between 30°N and 40°S only the most northerly and southerly ones show a pronounced oscillation, with a maximum in July-August and a slight minimum between November and March. Irregular fluctuations around an average value occur near the equator. Yearly fluctuations are observed, not only by the potential gradient, but also by the conductivity and electric charge in the atmosphere.

(3) *Eleven-year period.* L. A. Bauer (1924) was able to demonstrate a close relation between the number of sun spots and the potential gradient; the latter increases 20% with a 100% increase in the number of sun spots; the daily and yearly amplitudes of the potential gradient also fluctuate parallel to the curve of sun activity and seem to be related to the northern light phenomena.

The various characteristics of air conductivity and potential gradient were discussed at some length because a considerable amount of literature has been published on the possible biological effects of fluctuations in the potential gradient.

It should be realized that the potential gradient in buildings is zero, but, as we shall demonstrate presently, these fluctuations may correlate with certain meteorotropic phenomena for three reasons:

(1) As a rule a person will be outdoors during a certain part of the day, unless he is seriously ill. As clearly demonstrated in diuresis studies (see

p. 334), a short outdoor interlude of this kind (half an hour or more) is often sufficient to create a certain physiological effect. In other words, on days characterized by many hours of strongly fluctuating potential gradient (high positive and high negative), a person could be affected by the electric field of the atmosphere (assuming that such an influence exists), even if he stays indoors for a considerable part of the day.

(2) Days with considerable fluctuations of the potential gradient are usually marked by important changes of a number of other meteorological factors, such as conductivity and ionization of the air, temperature, air mass, wind speed, etc.

(3) As we hope to demonstrate later in this Part, a much-weakened version of changes in the macroclimate outside buildings usually is reflected, in the microclimate inside buildings. In other words, a strongly fluctuating potential gradient outside a building may correspond with sudden changes in air conductivity, air circulation or temperature inside the same building and it may be due to the latter changes that a given meteorotropic correlation is found between potential gradient and a certain clinical phenomenon.

5. *Methods of Recording*

Various types of instruments are being used by different meteorological institutes, the ordinary wire electrometer type (of Wulf) being the most common. It was found that this instrument is often rather slow in its recordings and the influence of air movement and other disturbing factors may be appreciable. Recently new electronic devices have been developed, *e.g.* by Reiter[55] and Koenigsfeld[46, 47]. The latter in particular, developed in the atmospheric electricity section of the Royal Meteorological Service at Uccle (Brussels) has proved to be extremely satisfactory. The potential difference between a point in the atmosphere and the earth's surface is measured with a radioactive electrode (*e.g.* Ra D) and an electronic microvoltmeter with high internal restistance (of the order of 10^{10} Ω). The recording is done with an automatically recording milliammeter (*e.g.* Brown or Metrawatt Recorder). The purpose of the radioactive electrode is to create a strong and constant degree of ionization at a fixed point in the air. Depending on the potential difference between this point and the earth's surface, a different ionic current ($\mu\mu A$) will flow through the microvoltmeter. This current is continuously recorded. In view of the very small current and leakages due to moisture, the cable, connecting the electrode and microvoltmeter, is made of several insulated layers, near the electrode (placed a few m above the ground) surrounded by a long, strongly insulating perspex tube (Nieuwendijk system) in order to minimize current losses. Accurate recording of the potential gradient is a complex problem, like ionization measurements, and the many records published in biometeorological literature should therefore be accepted only after careful analysis of the methods applied.

Subsect. C. ELECTROMAGNETIC LONG WAVES

It has been known for a considerable time that, particularly during the approach of deep depressions and storm centres, electromagnetic waves are emitted by these centres with wavelengths of 6–100 km and a frequency of 3–5 kHz. These E.M. waves are known in the German literature as Infra long waves. Reiter[455], König[44, 45], Schultze and Wedler, in particular, have stressed the possible biological effect of these waves, as they are able to penetrate into buildings.

H. König, physicist of the Meteorological Institute at Hamburg, developed special recording equipment which makes it possible to register these waves as electromagnetic impulses. The impulses are divided into two groups: those with amplitude 0.01V/m and others with 0.2 V/m. The impulses with amplitude 0.01V/m usually amount to several thousands per day; 0.2 V/m to only several hundreds.

The recording equipment consists of a radio aerial (a vertical pole of 3.30 m), an electronic magnifier (consisting of a three-stage waveband amplifier), an electronic E. M. impulse counter and a recorder (for both amplitudes). For further details see refs.[44, 45].

The daily number of impulses (both with small and large amplitudes) is relatively small during winter and increases suddenly around May and June. It reaches a maximum in August. In September it gradually decreases. The rate of decrease during the following months depends largely on whether winter starts early or late in that particular year.

In August 1956 the average daily number of impulses (at Leiden, the Netherlands) with amplitude 0.01 V/m amounted to 179,000/24 h, with amplitude 0.2 V/m 1300/24 h. In that year the lowest values were 12,000 (0.01 V/m) in December, 400 (0.2 V/m) in February and 600 (0.2 V/m) in December. During the abnormally warm year of 1959, in W. Europe a very large number of impulses was recorded which reached values of 650,000 impulses/24 h (*e.g.* on 8th July 1959). Values of 200–300 thousand impulses a day were very common in June, July and August 1959.

The number of impulses has a pronounced daily rhythm. From January till March a maximum occurs between 23 and 7 hours, a minimum between 10 and 16 hours. From May till August a second maximum occurs during the day (from 14–16 hours) apart from the night maximum. A minimum occurs at 8 hours. In general a sudden increase in daily number of impulses (0.01 V/m) indicates the rapid approach of an air mass with great atmospheric turbulence. As a rule warm tropical air mass influxes seem to be more often associated with a large number of impulses than polar air. However, many deviations from this rule have been observed.

Reiter[674] notably, in a series of excellent biometeorological studies in Bavaria, has come to the conclusion that at least in that area a number of highly significant statistical correlations can be observed between mortality, reaction speed, and a number of clinical phenomena and days with very high E. M. impulses.

In the Netherlands such correlations do not exist because the specific weather conditions which are responsible for certain meteorotropic phenomena usually occur several days after a peak in high impulses is observed. For example, near or during front passages the number of impulses in the Netherlands is usually very small. In Central Europe, however, these weather conditions are closely related to high impulses.

These observations strongly suggest that the E.M. impulses are valuable meteorological or biometeorological indicators, but there is probably only a statistical and not a causal relationship between these impulses and meteorotropism.

Section 8. Air Mass (Source and Properties)

On p. 17 the concept "air mass" and the differences in physico-chemical properties have been briefly discussed. In view of their great biometeorological significance, a little more should be said about these differences.

If the lower part of a moving mass of air is colder than the underlying surface, it becomes more unstable and cumulus clouds, showers and great turbulence become the normal accompanying phenomena. In the event of the air mass being warmer than the underlying surface, it becomes more stable, a fact which is indicated by low stratus clouds, fog or drizzle. In both examples it is not the absolute temperature of the air mass that counts, but the difference between it and the surface layer.

The first type is exemplified by the very cold, dry and stable polar air masses of N. Canada and Siberia, which become unstable as they move southwards. If cold polar maritime air (cold compared with sea water) moves inland in winter over very cold ground, it becomes quickly transformed into the second group and the initial instability changes into stable conditions. Nevertheless it usually contains enough moisture to produce rain if lifted several hundred metres.

Belasco[39] has given an excellent review of some of the meteorological characteristics of air masses over the British Isles which can be applied more or less to the major parts N.W. Europe. In a series of tables for 16 types of air masses the average, maximum and minimum temperature, average wet-bulb temperature and mean vapour pressure are given for various months of the year. Table 15 gives, at an elevation of 700 mb (roughly 2400 m), a number of conditions, observed in the principal groups of air mases.

TABLE 15

PRINCIPAL PHYSICAL CHARACTERISTICS OF AIR MASSES DURING SUMMER AND WINTER (ACCORDING TO BELASCO[39])

Type of air mass		Temperature °F mean	max.	min.	Mean vapour pressure mb	Mean wet-bulb temperature °F	Period of year
Tropical	maritime	41–44	45–49	37–41	4.3–5.0	61	summer
		29–33	34–37	25–30	3.3–3.9	55	winter
	continental	43	49	40	5.2	62	summer
		25	30	21	3.8	53	winter
Polar	maritime	19–29	22–32	14–26	2.8–4.3	47–55	summer
		−4/+16	1–20	−10/+12	0.8–2.6	30–46	winter
	continental	−8/−3	−4/−1	−13/−4	0.7–0.8	28–31	winter

This summary clearly indicates the great differences in temperature and moisture content between the different air masses and between different periods of the year.

A similar review concerning air mass differences in Central Europe was compiled by Dinies in 1932 (ref.[41]). Students in biometeorology are strongly recommended to study the original articles.

We have just mentioned differences in number of E.M. impulses with different air mass influxes. In Chapter 2 of this Part differences in ozone content (p. 89) and acidity (p. 98) of the air will also be discussed.

Section 9. Frontal Activity

The concept "front" and the various types of fronts were discussed on page 18. The biological effect of fronts, which is probably mainly due to the sudden changes of various physical (and perhaps chemical) factors in the environment after the passage of a front, greatly varies with what is termed the *activity* of the fronts.

The activity is usually determined by a number of factors, *viz.*:

(1) The speed of movement of the front, in other words the speed of environmental change.

(2) The degree of rise or fall of barometric pressure after the passage of a front. A sudden rise or fall is usually characterized by a sudden decrease or increase in wind speed and a change in wind direction.

(3) The degree of rise or fall of the temperature after the passage of a front.

(4) The degree of disturbance of the electric field of the atmosphere; during great frontal activity the potential gradient fluctuates between high positive and negative potentials.

(5) The amount and duration of precipitation.

The more predominant each of these factors is the more marked are the meteorotropic effects of these frontal passages likely to be.

Section 10. Interrelationship between Internal Microclimate of Rooms and Buildings and External Weather Conditions

Various studies have been carried out on the interrelationship between internal climate and external weather conditions. Most people are inclined to believe that in a well-built modern house or building sudden changes in weather conditions outside do not affect the internal microclimate. This, however, is not true and can be demonstrated in various ways.

Measurement of the electrical conductivity of the air

Schilling and Carson[108] carried out simultaneous measurements of the electrical conductivity of air inside and outside a building with two identical Gerdien tubes (see p. 74). The observations were made sometime in 1953 in a closed room on the 4th floor of a newly constructed campus building at the University of California (Los Angeles, U.S.A.).

The air was supplied by a ventilating system bringing outside air from the roof through oil-impregnated wire mesh filters into the room. Several persons worked in the room and smoked cigarettes during the experiment. The simultaneous recordings showed the following results:

(1) The general trend of the conductivity curve was the same in the building and on the roof.

(2) Both curves showed a diurnal variation.

(3) The conductivity, measured inside, was usually a little higher than the outside values.

(4) Occupancy of the room has a definite effect on the large ion concentration of the room but not on its air conductivity.

(5) Changes in conductivity are often observed in a room, hours in advance of approaching meteorological disturbances such as weather fronts.

Measurement of electric space charges

During thunderstorms or rain, considerable space charges are recorded in the atmosphere. According to Mühleisen[54], values of more than 2000 e/cm^3 have been observed. The electric charges are usually attached to water droplets of only a few μ in diameter.

Simultaneous recordings by Mühleisen (at the Max Planck Institut für Aeronomie, Weissenau, Germany) in the open air and in a closed hall of a building have shown the same fluctuations in space charges in and outside during changing weather conditions. Mühleisen assumes that the high electric space charges observed in buildings during thunderstorms did not penetrate through the walls but were due to very small charged particles which penetrate into buildings through tiny cracks in doors and windows. Here again a close relationship between the inner and outer environment was demonstrated.

Measurement of wall temperature and air movement

On p. 36 we pointed out that, during a sudden influx of cold polar air, for example, particularly if it is accompanied by rain and great atmospheric turbulence, the room temperatures of the outer walls of completely closed rooms or buildings may drop suddenly several °C. This is due to the strong cooling of the wet walls in the open air, particularly as a result of considerable air movement and evaporation of moisture on the walls. The suddenly increased radiation loss of the body of a person sitting near such a wall will be experienced physiologically by this person. In other words, the change in weather conditions outdoors, even if the air temperature in the closed room is kept very high, will be noticed by people living in such a room. Furthermore, considerable air movement is perceptible near windows and doors, even in modern buildings, which creates a chilling effect on the body.

Measurement of air exchange

M. von Pettenkofer pointed out more than a century ago (1858) that a regular exchange takes place between the air in an inhabited room rich in CO_2 and the free atmosphere. In his view this exchange takes place through the porous walls of the rooms (*wall breathing*). Others are more inclined to believe in an exchange through cracks near windows and doors, etc. Hottinger[103], Courvoisier [99], Küster[105], Georgii[102] and others observed in a series of experimental studies that, with wind speeds of 6–7 m/sec, the air of a room is as a rule completely replaced by fresh air within about one hour, a process known as *autonomous air exchange.* With wind speeds of 2–3 m/sec, only about 0.4 of the room air will be replaced. This process depends mainly on three factors, *viz.*:

(1) *Pressure difference in the air on the wind and lee side of a building.* According to Hottinger[103], the total pressure force on the lee side is

$$p = 0.8\ V^2 \rho$$

where V = wind speed in m/sec and ρ = 1.2 kg/m³. Two-thirds of this pressure are roughly equal to the section force in the lee area itself.

The pressure force with wind speed 1 m/sec = 0.007 mm Hg, 2 m/sec = 0.029, 3 m/sec = 0.063, 4 m/sec = 0.12, 5 m/sec = 0.175, 6 m/sec = 0.26, 7 m/sec = 0.35, 8 m/sec = 0.44, 9 m/sec = 0.56, 10 m/sec = 0.68, 20 m/sec = 2.8 (according to Georgii).

As a result of these pressure differences the air exchange in buildings is stimulated.

(2) *Difference in temperature between room and outer atmosphere.* Warm air of the room is rising and cold air is coming in at floor level. This creates small pressure differences:

$$\rho = h\ (\rho_c - \rho_w)\ \mathrm{g/cm^3}$$

where h is the height of the plane of equilibrium in the room, ρ_c and ρ_w = density of the cold air outside and of the warm air inside respectively. In a room 3 m high, with h = 1.70 m, recordings by Ilzhöfer[104] have shown that, with a temperature difference of 1°C, the pressure difference will be only 0.0005 mm Hg, 5°C = 0.0028, 10°C = 0.0056, 15°C = 0.0084, 20°C = 0.012.

In the case of a deep cellar, connected with a high staircase in a hall, the value of h in the formula may be 10 times larger and the pressure values given above will also therefore be 10 times larger. However, in rooms on higher floor levels in a building the temperature factor for an exchange is very small and it is the wind effect which proves to be a dominating factor.

(3) *Diffusion of gases or trace substances with different concentrations inside and outside buildings.* In 1951 Georgii studied this problem at the Meteorological Institute of Frankfurt (Germany) in a rectangular room of 32 m³ on the second floor of the building. All cracks near windows, doors, etc. were carefully sealed. Doors and windows remained closed during each four-

hour experiment (for further details see ref.[102]). The CO_2 concentration of the room was increased artificially and the gradual decrease was recorded. In view of the very low CO_2 concentration in the free atmosphere (see p. 87) this method is fairly trustworthy, the more so as experiments have shown that older cement or concrete walls in buildings cease to form a chemical compound with the CO_2 of the room.

In Georgii's CO_2 experiment it is difficult to make out whether the exchange took place through pores of the walls or through cracks near windows, etc. Georgii therefore introduced the *aerosol method*. Unlike CO_2, the concentration of aerosols (see p. 101) can only decrease by virtue of actual air exchange through cracks. 1/500 normal $CaCl_2$ spray was used as the aerosol.

Both the CO_2 and aerosol method showed the same exponential concentration decrease with time. The total decrease during a certain time interval is different on different days and greatly depends on the velocity of the wind and temperature difference. According to Georgii, the stationary gas exchange in a room (S) is, at a temperature of T °C:

$$S = 2.302 \frac{V}{t} \log \frac{C_1}{C_2}$$

if V = wind speed, t = time, C_1 = concentration of gas at the moment t_1, C_2 concentration of gas at the time t_2.

With $V = 0$, the air loss is about 2.5 l/sec which seems to be due to diffusion through the wall and through little cracks in windows (according to Georgii). With increasing wind velocity, S increases rapidly owing to actual air replacement.

With increasing CO_2 content of the air in the rooms (*e.g.* if many people are sitting in the room) the N_2 and O_2 concentration will be less than outdoors. Diffusion and autonomous air exchange will gradually bring more O_2 and N_2 into the room.

Further experiments have shown that the smaller the rooms are, the greater, usually, is total air exchange. Wooden floors permit greater exchange than linoleum floors, etc. Buildings along streets with heavy traffic will suffer more from minor cracking and, as a result, the processes mentioned above may be more pronounced. It is evident that the position of the building in relation to the dominating wind direction is likewise important. All these problems will be discussed in greater detail in Part IV, Chapter 3 (Urban Biometeorology).

The foregoing summary clearly indicates the close relationship between the internal and external environment of buildings. Most people will spend at least a few hours of the day in the external environment and will therefore be subjected to the influence of the daily changes in the weather. But, even if a person stays at home, he always experiences physiologically the changes in the outer environment. This is a most important fact which we must keep in mind in the next chapters. In this connection the following studies by Landsberg are of particular interest.

H. Landsberg* studied during 100 nights (Sept.–Dec. 1937) the relationship between outside temperature and bed temperature. The former fluctuated between +17 and —14° C. As during 75% of the days the difference between the temperature of the room (with an open window) and the bed temperatuıe is 7.6–12.5° C, a consideıable amount of energy is required by the thermoregulation centres of the body (see p. 232) to keep the bed temperature at a constant level. This explains various physiological experiences of rheumatics during cold and humid nights (see p. 550). It also demonstrates that for many people a warm bed is not a sufficient protection against meteorotropic influences.

* H. Landsberg, Eine Bett-Temperatur Studie, *Bioklimat. Beiblätter*, 5, 2, 66–68(1938).

CHAPTER 2

Chemical Factors

Section 1. Normal Chemical Components of the Atmosphere

The atmosphere is made up of a mechanical mixture of different elementary gases: nitrogen (78.08%), oxygen (20.95%), argon (0.93%), neon (0.0018%), helium (0.0005%), krypton (0.0001%), hydrogen (0.00005%), xenon ($8 \cdot 10^{-6}$ %), ozone ($1 \cdot 10^{-6}$ %) and radon (*i.e.* radium emanation, $6 \cdot 10^{-18}$ %). Except for ozone (O_3) and radon (see p. 652), these percentage are practically the same throughout the atmosphere, at least to 150 km altitude. Only the partial pressure is different at different altitudes (see p. 293).

The ozone content increases with height and reaches a maximum in the warm layer of the stratosphere at an elevation of about 22 km (see p. 22)*. Contrary to ozone, the amount of radon decreases with height.

Apart from the gases mentioned, the atmosphere contains carbon dioxide (0.03%) and particularly large masses of water vapour. The latter is important for the transportation of water through the atmosphere and because of its capacity to absorb infrared solar rays with a wavelength longer than 800 mμ. On a clear humid day it absorbs less than 15% of the sun's rays. However, it absorbs the infrared terrestrial radiation of the soil ($\lambda = 4$–50μ) almost completely. If the partial water vapour pressure at sea level is considered to be 1, it is only 0.68 at 1 km altitude, 0.41 at 2 km, 0.11 at 5 km, 0.013 at 8 km (according to A. Wegenet).

Carbon dioxide is also an important heat regulator of the troposphere. It has the capacity to permit the sun's rays to reach the earth's surface but absorbs the reflected heat rays. Although at present the amount is estimated to be 0.03% (according to Kreutz[185], near the earth's surface 0.0438 %), it may have been considerably higher in many parts of the world during geological periods of volcanic activity. According to a theory of Arrhenius[111b], an increase of CO_2 in the atmosphere to 0.08% would increase the arctic

* Even in this *ozone layer* or *ozonosphere* the ozone concentration is only 1/5 p.p.m. The ozone in the higher atmosphere is produced by irradiation of oxygen molecules by ultraviolet light in the region between 10 and 50 km above the earth's surface. The irradiation produces oxygen atoms (O) which unite with oxygen molecules (O_2) to form ozone (O_3). Above 50 km the oxygen becomes too diffuse. Below 10 km turbulence of the air will bring small amounts of O_3 to the earth's surface.

temperatures by 8–9° C, a decrease in CO_2 to 0.015 % would lower the temperatures at 45° latitude by 4–5° C. More recent studies by Angström[111a] and Rubens and Ladenburg (1905), however, have shown that this assumption of Arrhenius is not correct. An increase in CO_2 has no effect, a decrease only below 1/5 of the present value could have a certain influence.

The great constancy of CO_2 content of the atmosphere was demonstrated by Carpenter in 1937. Eleven hundred analyses of outside air in New Hampshire (Boston) and Baltimore (U.S.A.) gave the same CO_2 concentration of 0.03%. This value did not change during the different seasons or from year to year.

Section 2. Trace Substances of the Atmosphere[112–154]

Subsect. A. OZONE (O_3)[122–154]

Although most people are well acquainted with the characteristic fresh and penetrating odour of this gas, which is often noticed after electrical discharges in the laboratory or in nature after lightning storms, still very little is yet known about its real biometeorological significance. It is employed for purifying and deodorizing air in buildings or underground railways, for sterilizing drinking-water, etc. In other words, there is no doubt that, in larger concentrations which we can smell, O_3 has a biological effect. In Nature, near the surface of the earth, the concentrations are quite small.

It is chiefly due to the studies of the German scientists, Cauer[126], Daubert, Effenberger and Warmbt[154] that we know considerably more about the distribution of ozone in the lower atmosphere of Central Europe and the meteorological factors affecting this distribution. According to Cauer and Effenberger, the ozone content varies between 20 and 50 γ/m^3. It is higher above the sea than above land and usually increases with rising temperature and falling humidity.

Meteorological factors affecting the distribution of ozone in W. Europe

(1) The ozone content of the air has a daily rhythm usually with a maximum around 2 p.m. and a minimum at 8 a.m. In May and following summer months daily fluctuations up to 14 γ (21 γ against 35 γ) have been observed, the differences being small in winter (only few γ).

(2) Ozone content is very low (particularly in winter) on land under stagnant air conditions, with fog and during "inversions" (see p. 19); it increases with increased turbulence and thermal convection in the air (particularly in summer).

(3) Days with high atmospheric pressure (in W. Europe often accompanied by fog and inversions), too, have low ozone values, whereas days with thunderstorms, lightning and snowstorms have high values.

(4) The ozone content also varies with the dominating direction of the wind. In N.W. Germany (according to Effenberger) the average O_3 content with east wind is 29.9 γ m^3, with a west wind 42.6 γ, with a south wind 51.4 γ, with a north wind 41.3 γ. The low value with an east wind, due to the low ozone content of continental air masses in W. Europe, is partly the result of the oxidizing effect of plants and forests in Central and Eastern Europe.

(5) In winter the ozone content is usually lower than in summer, but air mass influxes may change this rule completely.

(6) High ozone values are usually observed in N.W. Europe during the passage of cold fronts and the influx of polar air masses, whereas warm fronts with tropical air are usually characterized by low values.

TABLE 16

OZONE CONTENT OF DIFFERENT AIR MASSES IN W. EUROPE (AVERAGEVALUES IN γ/m^3)

Air mass	*Winter*	*Spring*	*Summer*	*Autumn*
Polar maritime air	22.5	26.6	25.9	20.6
Polar continental air	5.9	13.8	13.3	5.6
Polar maritime air (considerably altered and heated)	11.6	18.1	27.8	18.1
Continental air	0.8	16.9	29.3	11.6
Tropical maritime air	14.2	23.5	27.9	17.2

(7) Daubert, using Ehmert's ozone recorder, made over 16,000 ozone recordings in the period 1950–1954 in relation to air masses in W. Europe. Table 16 gives the average values in γ / m^3 (written information).

(8) Other studies by Daubert revealed that the frontal part of approaching depressions have low ozone values, whereas the high values are found on the back, particularly in summer.

(9) In humid air (far below the saturation point), with sufficient condensation nuclei, ozone accelerates fog formation (experiments by Cauer).

(10) Experiments by Heinke and Herrmann[136] suggest that the acidity of the air increases with increased ozone content of the air.

Influence of ozone on atmospheric pollution

Since the Second World War, particularly, the population of Los Angeles (U.S.A.) has been suffering from heavy smog (see p. 19), which will be discussed more fully in Chapter 4, Sect. 6 (p. 142). During such periods the population suffers from inflammation of the eyes and of the mucous membranes of nose and throat; plants and vegetables suffer heavily; small cracks appear in vulcanized rubber (*e.g.* of cars).

Haagen-Smit was able to demonstrate that this smoggy atmosphere is rich in oxidizing substances and organic material which derived from decomposed hydrocarbons. One of the most important oxidizing substances of smog proves to be ozone. Owing to the oxidation of hydrocarbons, a great variety of substances are formed such as peroxides, aldehydes, butenes, nitric acid, etc., which are responsible for the irritation of the membranes of nose and throat.

Studies by Haagen-Smit[133, 134], Littmann, Ford and Endow[140] have shown that ozone is practically absent during the night but is formed by sunlight as a result of the following chemical reactions: Owing to exhaust gases (see p. 96) of the more than 2 million cars of Los Angeles (producing about 1000–1350 tons of hydrocarbon losses) nitrogen oxide (NO) is formed. With light waves shorter than 3600Å, NO_2 is formed in the presence of organic substances. NO_2+active hydrocarbons+light produce O_3. According to Haagen-Smit, the presence of alkyl or aryl groups in the hydrocarbons increases the ozone formation considerably. On the other hand, SO_2 and NO_2 in a smog area may reduce the ozone concentration, because these substance are oxidized by O_3 into H_2SO_4 and NO_3.

Biological effects of ozone

Comparatively few physiological studies have been made on the direct biological effect of ozone on human health. The first extensive study was made in 1911 by Hill and Flack[137] in the Laboratory of the London Hospital Medical College. Their observations were confirmed in the U.S.A. by Jordon, Carlson and Sawyer in 1913. Up to his recent death, Curry[4] defended the theory that most meteorotropic effects are due to an unknown gas which he called "Aran", apparently similar to ozone. It is for this reason that a fairly detailed summary will be given of the known biological effects of ozone.

(1) According to studies made by Schwarzenbach, Barlow, Filipow, Schulz, Bohr and Maar, at the beginning of this century, ozone causes *irritation and oedema of the lungs* and ultimately *death if inhaled in strong concentrations.* With concentrations of 0.05%, death follows in 2 hours, with 1%, after one hour. Experiments by Bohr and Maar in 1904 showed that with ozone concentrations which do not produce changes in pulmonary structure, the uptake of oxygen and output of CO_2 is diminished both in

cold and warm-blooded animals. The effect on the CO_2 output is less than on the O_2 uptake. With weak concentrations of ozone the respiratory effects reached their height after the cessation of ozone inhalation. This effect was not modified by a preliminary division of the vagi and pulmonary sympathetic nerves (see p. 189). The blood of the ozonized animal has no toxic effects when transfused into another.

(2) Studies by Butte and Peyron (in 1894) suggest that ozone inhalation *diminishes general metabolism* in concentrations less than 4000 γ/m^3 and lowers the body temperature.

(3) According to Binz (in 1882), animals submitted to ozone become *quiet and drowsy* due to decreased respiratory exchange. His observation was confirmed by Sigmund in 1905, who made similar experiments with white mice, goldfish and insects.

(4) Hill and Flack refined the laboratory methods by using as pecially constructed ozone generator consisting of sheets of fine gauze set parallel and insulated from each other. Electric discharges of high-potential currents across the gauze developed pure ozone and prevented the formation of nitrogen oxides, as often happened in older experiments. According to Berg[123] and Cauer[126], nitrogen oxides and the organic products oxidized by ozone, seem to be mainly responsible for the actual smell of ozone and may explain why the smell may persist, even if the ozone concentration drops to zero (Berg's experiments). The ozone concentration in the air was measured by sucking 10 l of air through a 1% solution of potassium iodide. After adding pure starch emulsion, the intensity of the blue colour can be estimated by titration (for further details see ref.[126]). Animals were placed in large airtight chambers (with glass windows) through which the ozonized air was pumped.

It was found that animals die after 2 hours when submitted to ozone concentrations of 15–20 p.p.m. Lower concentrations may have the same effect if applied for longer periods, causing coughing and headaches.

The cause of death seems to be acute inflammation of the respiratory tract. The lungs become congested and oedematous; the pulmonary alveoli are full of an inflammatory exudation. Many alveoli are full of blood. There is no evidence of ozone in the exhaled air; it is all absorbed by the wet mucous surface of the respiratory tract.

Breathing air with ozone 2–3 p.p.m. causes only irritation of the respiratory tract. 1 cm^3 of ozone weighs 2.143 mg (against 1.429 in the case of oxygen and 1.293 of ordinary air). Therefore a concentration of ozone 2 p.p.m. equals 4.29 mg O_3/cm^3 or 4290 γ/m^3, which is more than 80 times the usual amount of ozone in the air. Even below the concentration of 2000 γ/m^3, one can still smell ozone.

In small quantities O_3 stimulates the olfactory nerves and the nerve-endings in the respiratory tract, which seems to relieve the monotony of the microclimate in closed rooms with constancy of temperature, humidity and lack of air movement.

Due to its oxidizing properties, O_3 is able to destroy bacteria and noxious gases, particularly in the presence of water vapour.

Exposure of rats to air with 430 γ/m^3 (for 10 min) lowered the rectal temperature by 3° C.

(5) Heinke and Herrmann[136] observed *changes in potassium and calcium level of the blood serum* of persons introduced into artificially ozonized rooms. Ozone was produced each morning by a mercury low-pressure discharge lamp (type HNS 10, Osram) in a closed room from 5 a.m.; at 8 a.m. a venous blood sample was taken before the patient had had breakfast. Forty people in all were tested in 11 rooms of the Dermatological University Clinic at Giessen (Germany). The normal ozone concentration was 0–5 γ/m^3, after using the Osram lamp, 30–90 γ/m^3. An increase in potassium was observed after 3 hours of ozonization in 72% of the cases, and a decrease in calcium level in 70% of the cases. This observation is of particular importance because an increase of the K/Ca ratio may cause an augmentation of irritability, not only in the heart muscles but also in the skeletal muscles. Under extreme conditions it may even lead to a tetany.

The decreased calcium level might be the result of dysfunction of the parathyroid gland (see p. 275), which is controlled, at least partly, by hormones from the anterior lobe of the pituitary (see p. 257). However, the actual physiological mechanisms involved in ozonisation are still unknown.

The studies of Herrmann and Heinke are particularly important, because the concentrations of ozone being used, although higher than usual in the atmosphere, were relatively low.

(6) In 1958 studies were carried out in the U.S.A. by Miller and Ehrlich[141] on the *susceptibility to respiratory infections* of animals exposed to ozone. This study was stimulated by the present trend in aviation towards flying at high altitudes, where high concentrations of ozone occur. Previous studies by Mittler *et al.*[142,143] at the Armpur Research Foundation have shown that 50% of a group of mice were killed after a three-hour exposure to ozone of concentration 12.6 p.p.m. For rats this lethal dose is 13.1, for rabbits 21.6, for Guinea pigs 30.1, for hamsters 35.5. Death was always due to haemorrhage and oedema in the lungs. Exposure of rats to ozone concentrations of only 2.4 p.p.m. had the same effect after 64 hours. Miller exposed approximately 300 Swiss albino mice and 150 hamsters to sublethal concentrations of ozone and various infectious agents. Four types of experiments were

carried out: 3 hours' exposure with ozone concentrations 3.6–4.9 p.p.m.; 3 hour's exposure with O_3 concentrations of 0.96–1.7 p.p.m., 4 hours a day for 5 days per week for 2 weeks with concentration 0.3–1.2 p.p.m., 100 hours with a concentration of 0.3–1.1 p.p.m. O_3. The micro-organisms used for infection were various strains of *Klebsiella pneumoniae* and *Streptococcus*. The experiments have given the following results:

Exposure to ozone lowers the resistance of mice and hamsters to respiratory infections caused by *K. pneumoniae* and *Streptococcus*.

Mortality is increased and survival time of these animals is shortened. These relationships proved to be statistically significant for most experiments at the 0.1%-level.

(7) Further evidence is found of the *biological effects of ozone in plants* growing in air-polluted areas.

Haagen-Smit[134,135] and Haagen-Smit *et al.*[176] were able to demonstrate that 0.2 p.p.m. ozone together with 2–7 p.p.m. of certain hydrocarbons (particularly unsaturated ones) produce various products (such as hexenes and nonenes) which are highly toxic to plants. Ozone alone or only hydrocarbons had no effect.

An interesting observation was made by Haagen-Smit, *viz.* that traces of SO_2 (0.1 p.p.m.) prevent this toxic activity of "smog" air.

Experiments by Middleton[196] have shown that these toxic substances in aoncentrations which do not cause visible changes in plants, nevertheless effect plants in their growth and the production of seeds, etc.

Recent studies by Heggestad, Middleton[196] and Wanta[153] point to the effect of ozone on tobacco leaf. In the U.S.A., in Connecticut valley, at Beltsville (Md.), in North Carolina, in Ontario (Canada) and in other places tobacco leaf damage, known as *weather fleck,* often creates a serious problem in the production of cigar-wrapper tobacco. Rubber strip tests and an ozone recorder indicated that highly significant correlations existed between ozone and the appearance of weather fleck during periods of abnormal concentrations of ozone. Artificial ozone in climate chambers produces the same effect. Similar damage is observed on the upper-leaf surfaces of beans and grapes. Whereas toxic products of the oxidation of hydrocarbons during smog inflict damage on the lower leaf surface, ozone damage appears on the upper-leaf surface only. Although average values did not exceed 6 parts per hundred million, maximum values of 50 p.p. 100 m. were recorded during certain sunny warm periods of the day. Certain species have a threshold value of 20 p.p.100 m. for 3 h of exposure before fresh damage develops.

This summary of the biological effects of ozone is far from conclusive, because several experiments were carried out with high concentrations of ozone. Only the experiments by Heinke and Herrmann and the plant experiments approach the atmospheric conditions. However, in view of the data given above, it is difficult to believe that a sudden increase in the ozone content of the air from 1 to 30–50 γ/m^3 would not have certain biological effects on the respiratory system. More experiments under strictly controlled conditions are required to clarify this matter.

Irrespective of the outcome of future studies and in spite of its extremely small concentration, ozone will always be of the utmost importance to living organisms on earth. Without ozone, the ultraviolet radiation of the sun would cause sunburn at least 50 times as intense as that observed during the summer on high mountains. Nor could the eyes of animals and man have been developed in their present form in the course of geological history. If the ozone concentration were to increase too much, there would ensue a catastrophic reduction in the ultraviolet radiation received on earth. Below a certain ultraviolet level, the production of vitamin D would cease and the bones of animals and man could not develop properly.

Subsect. B. SOIL GASES

A great variety of gases may occur in the soil and the atmosphere immediately above it.

In *volcanic regions,* apart from great quantities of water vapours, the soil vapours are usually rich in the following gases: H_2S, SO_2, HCl, Cl_2, CO, CO_2, CH_4, H_2, N_2, O_2, H_3BO_3, Fe_2Cl_6, H_2SO_4 and NH_3.

In *non-volcanic sedimentary regions* different gases are found in the lower parts of the atmosphere, depending on the type of soil sediment.

In regions rich in organic sediments (peat soils, coal and oil deposits) or marsh land various organic gases are found. Near *oil seepages* traces of various hydrocarbons occur of the general formula C_nH_{2n+2} of which methane (CH_4) may be present in great abundance (80–100% of the earth gases). Other hydrocarbons which have been found are: ethane (C_2H_6), propane (C_3H_8), butane (C_4H_{10}), pentane (C_5H_{12}), hexane (C_6H_{14}) and heptane (C_7H_{16}) CO_2 (0–30%), N_2 (less than 1%), O_2 (0–0.2%), H_2S, traces of olefines (C_nH_{2n}), CO and H_2. In a few areas 97% N_2 has been reported immediately above the soil. In certain oil regions helium (up to 2%), with traces of neon and argon, may occur. In *marshy regions,* due to anaerobic fermentation of carbohydrate material of plants, methane is formed in great quantities. Traces of phosphine (PH_3) together with P_2H and P_2H_4 are formed in marshes out of bones and organic acids. This gas mixture is self-igniting in the air and burns into P_2O_5. Self-ignition of PH_3 causes ignition of methane and gives rise to the "will-o'-the-wisp" in marshy regions.

In regions composed of *non-organic, mechanical sediments* (sandstone, sand clay, marl,etc.) the volatile soil gases are usually formed by the decomposition of plants. Along footpaths crushed plants, moulds, fungi, toad-stools and soil bacteria create odorous substances which enable dogs to follow a track. These odours are absorbed in porous soil, especially on days of high atmospheric pressure, and are released during falling atmospheric pressure and rising temperature*.

Near ditches and canals with considerable H_2S development in mud by sulphur bacteria, a sudden fall in barometric pressure releases those gases which are distributed up to a considerable height above the soil. Moulds may cause a strong smell underneath the floors of old damp houses and may be partly responsible for certain allergic symptoms presented by the occupants. The soil odours are preserved longest if soil is covered by high vegetation and if the atmosphere is rather humid. However, a dry atmosphere, strong winds and intensive solar radiation soon dissipate the odours. Light rain may favour the release of soil gases, heavy rain soon drives off all soil odours. Although the factors described are usually unobtrusive in high modern buildings, all these volatile substances in the micro-atmosphere above most rural areas and less up-to-date cities may have certain biological effects, particularly in people with a very sensitive olfactory nervous system.

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* In a recent publication Went[216] pointed out that, whereas most plant products, such as carbohydrates, fats and protein, are decomposed in nature into CO_2 and H_2O, the derivatives of isoprene (terpenes, carotenoids, phytol, etc.) are not broken down as far as we know. Neither the temperatures in the atmosphere nor the known plant enzymes and micro-organisms are able to decompose these latter compounds. Only the carotenes in leaves, dropped off plants in autumn, may decompose, if exposed to the air, into *ionones* (with a strong odour) which evaporate.

Went estimated that the 10^7 km^2 of coniferous forests on earth would release per year $5 \cdot 10^7$ tons of terpenes into the atmosphere. The amount of volatile hydrocarbons from other plants is about the same amount. So the total amount of volatile organic matter which is released each year into the atmosphere is about 10^8 tons. They cause the typical smell of steppes, meadows, forests, etc. and are responsible, according to Went, for the *blue haze* formation during daytime above vegetation areas. This results from photochemical oxidation of the organic vapours. A similar process was discovered by Haagen-Smit in the smog areas (see p. 90) where the ultra-violet or visible sunlight in the presence of nitrogen oxides decomposes very low concentrations of olefines in the atmosphere, releasing peroxides and ozone. At the same time, condensation occurs and larger molecular aggregates are found. The blue haze is caused by the Tyndall effect, which is due to the reflexion of predominating blue light against particles of less than $0.1\,\mu$ diameter.

Subsect. C. AIR-POLLUTING GASES[155-218]

The presence of air-polluting gases in the atmosphere and their biological effects will be fully dicussed in Chapter 4 (p. 116). Industrial exhaust gases are the main source of these air-pollutants. There is, however, another group of exhaust gases which may become a biological danger, at least in the larger cities. A few general remarks should be made on this particular group of gases in the lower part of the atmosphere, *i.e.* gases due to motor traffic[155-218]. They are in part hydrocarbons related to gasoline and in part are broken down into a series of cracking products. Apart from CO_2, H_2O, pure H_2 (from 1-3%), CO (up to 4%), aromatic substances, adehydes (*e.g.* CH_2O), considerable quantities of nitrogen oxides (such as NO), alcoholic substances (up to 0.01%), SO_2 (0.07%) and H_2S (0.01%) have been found. The biological effects of the latter two are briefly discussed on p. 499. Also lead products used in present-day motor spirit (about 0.4 ml/l) reach the atmosphere in the form of small crystals of $PbCl_2$ and $PbBr_2$ (of 2–100 mμ). According to Preis[203], in Zürich (Switzerland) the average lead content of air amounts to 2–5 γ/m^3, in traffic tunnels 20 γ/m^3, in garages as much as 40 γ/m^3. In Los Angeles[166] on clear days the Pb content is 2 γ/m^3 (with CO 3.5 p.p.m.), on "smog" days 42 γ Pb/m^3 with 23 p.p.m. CO.

This summary shows that CO is the most abundant exhaust product, its toxic effect being generally known. According to Wilkins[217], the CO content in the streets of Los Angeles amounted in 1956 to 58–160 parts p.p.m.; in London it was 1–50 p.p.m. (average 15). The concentration decreases with height. For example, in the centre of London 10 p.p.m. were formed at 4 ft. against 3.2 p.p.m. at 100 ft. This supports the view that the main source of CO is road traffic and not chimney smoke. It is interesting to note that, during the heavy smog period in London of 4–7 January, 1956 (see p. 19), the average CO concentration amounted to 8 p.p.m. only, probably due to the greatly reduced road traffic. With ordinary traffic in W. Europe the CO content is on an average 5–20 p.p.m.; with heavy traffic 50–80 p.p.m. In tunnels for road traffic it may increase to 600 p.p.m.

In contrast to gasoline traffic, the CO production in exhaust gases from diesel engine, traffic is very small or non-existent. The hydrocarbon content is also low. On the other hand diesel engines produce large amounts of soot and other odorous substances which are often irritating to the nasal and laryngeal mucous membranes and increase smog conditions at low level in the atmosphere. Owing to incomplete combustion of gasoline, acetylene and other related compounds are formed which, on account of high pressure in the diesel engine, are transformed into polycyclic compounds (arenes).

such as pyrene, fluoranthrene, 3,4-benzpyrene, 1,12-benzperylene, anthanthrene and coronene.

It is known that 3,4-benzpyrene in particular has *carcinogenic properties* if applied to the skin. Waller[212-215] found in various cities in the United Kingdom an average 3,4-benzpyrene content of 1–5 γ/100 m^3. Kotin[178-184] found 3 γ benzpyrene/100 m^3 5 m above the ground in Los Angeles on smog days. The amount fluctuates with the seasons. In London, 25 m above the street, the content in summer is 2 γ, in January 15 γ/m^3. In Sheffield during heavy fog in February, 33 γ/100 m^3 was measured. A similar seasonal fluctuation is found in the atmosphere in the floating soot, which contains 100 p.p.m. benzpyrene in summer against 300 p.p.m. in January. This would suggest that the heating of buildings in winter is partly responsible for the high winter values. According to studies by Kotin[182], the chief producer of benzpyrene is the lighty loaded, petrol engine running in low gear. Diesel engines produce little or no benzpyrene, provided there is complete combustion. Otherwise these engines also produce benzpyrene. Another important meteorological factor in the benzpyrene problem is the influence of light. Benzpyrene is very stable in dark surroundings, but quickly decomposes in sunlight. The presence of oxidizing substances like ozone (see above) also accelerates decomposition.

Subsect. D. IODINE, MAGNESIUM AND SALT

The atmosphere usually contains traces of iodine, magnesium chloride and salt (NaCl), all three important compounds which may affect the thyroid gland and nervous system of the human body.

The presence of salt is particularly noticeable on foggy days near the coast, when electric instruments in the open air show very considerable losses of current due to decreased insulation. The salt dissolved in the water droplets changes the water into a good conductor.

Cauer[115, 116] has considerably increased our knowledge of the daily fluctuations of various trace substances in the atmosphere and their possible biological effects by a series of studies conducted in Germany during the last 25 years. As several trace substances occur in the form of *aerosols*, their physical properties and biological effects will be discussed more fully on pp. 102 and 103. We shall discuss some of the results of Cauer's studies now.

(1) Cauer was able to demonstrate that in W. Europe most of the *iodine* in the atmosphere does not originate from evaporating sea-water but is due to the burning of large masses of seaweed rich in iodine, as is customary in various coastal areas of W. Europe: Brittany (France), Shetland Isles,

Stavanger area (Norway), area near Coruña (Spain), N. and W. coasts of Eire, but also along the Black Sea coast and in the Kola Peninsular. The seaweeds contain 0.0008–0.0012% of their dry weight in iodine.

(2) The iodine of the air is carried with various air masses as far as Central Europe. On the French coast (in Brittany) the average iodine content is 0.4 γ/m^3. Shortly after the large-scale burning of seaweed in this area it increases to 6000 γ/m^3. In Central Europe the average content is at present 0.05 γ/m^3, but up to 1934 (after which date Chile salpetre production caused a heavy drop in the world market price of iodine), it was much higher (0.6 γ/m^3). During periods of weed burning along the coast of W. Europe and strong air mass influxes over the European Continent it rapidly increases to 0.6 γ/m^3. Calculations suggest that iodine which actually originated from evaporated sea-water is only 0.0025 γ/m^3 (in Central Europe).

(3) Polar continental and polar maritime air masses are usually poor in iodine. Tropical maritime air usually has the highest values.

(4) In foggy areas volatile iodine in the air rapidly decreases, but is concentrated in the water droplets[112].

(5) Solar radiation together with ozone usually oxidizes the iodine ions in the water droplets into volatile iodine pentoxide.

These various factors explain the great variety in concentration of iodine in the air.

Few accurate data are available on the *magnesium chloride* content of the air. According to Cauer[116] the average content is about 3.1 γ/m^3 with a maximum of 65 γ/m^3. The main source seems to be evaporating sea-water and strong west winds (at least in W. Europe) which carry those water droplets far inland.

Subsect. E. ACIDITY OF THE AIR

Cauer[219] made many recordings of the differences in acidity of water droplets in fog and rain, varying between 2.6 and 7.2 At high altitudes in Central Europe pH values less than 2.7 were recorded (average 3.4), which is considerably higher than in the coastal plains of W. Europe. According to Cauer, this may have a lethal effect on bacteria at high altitudes.

Near the coast pH values of 4.6–5.2 were found, although even values of 3.8 were observed, which Cauer attributes to HCl formation above the sea due to oxidation of NaCl with ozone under the influence of solar radiation.

Cauer also observed increased acidity of the air in N.W. Germany (Norderney) with a sea wind. The different air masses are in all probability characterized by different acidities, but a systematic study has not yet been pursued. We mentioned on p. 89 that an increase in acidity is often observed with increased ozone content of the air.

Three important biological effects have been reported in relation to acidity of the air. The acidity can be due to HCl, HNO_3, H_2SO_4, organic acids and so forth.

(1) Studies by Tiefensee[1918] and others (see p. 475) suggest a decrease in attacks of asthmatic patients if aerosols with high acidity are inhaled.

(2) Statistical studies by Pemberton and Goldberg[201] have shown a steady increase of bronchitis, from rural areas to the cities and conurbations in the counties of England and Wales. Studies by Amdur, Melvin and Drinker[155] in Boston (U.S.A.) have shown that inhalation of SO_2 in concentrations of 1–8 p.p.m. increases the pulse and respiratory rates and decreases the tidal volume (respiration increases 3–4 breaths/min; pulse rate increases 8–9 beats/min; vol. decreases 25% during the first two minutes of exposure)*. Cralley[187] showed that higher concentrations inhibit ciliary activity in the human trachea. Using this information, Pemberton was able to demonstrate that a statistically significant correlation exists between average sulphur dioxide content of the air (*i.e.* also its acidity) in the different counties and mortality rates for bronchitis in men aged 45 and over (period 1950–1952). However, more recent studies in 1955 by Lawther[187], both in London and in the rural area of Kent, did not confirm the results of Amdur. The changes in respiratory rate, pulse rate, etc. were not consistent and therefore not statistically significant. Still, in 2 persons the application of 10 p.p.m. SO_2 caused severe bronchospasm.

(3) Studies by Heinke and Herrmann[221, 222] have shown a relationship between the pH of condensation nuclei in the air and the acidity of the skin surface. These conclusions were based on more than 2000 skin measurements during the period autumn 1948–summer 1949. The condensation nuclei were collected on the cold, chromium-plated, outer wall of a metal globe filled with ice (Cauer's method). The acidity of the skin increased with increased acidity of the air. This was particularly true in the case of patients suffering from eczema. It cannot be a direct effect, because non-living objects do not show a similar reaction. As sudden changes in activity of the autonomic nervous system (see p. 189) may alter the acidity of the skin consider-

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* Exposure of people working in industries, who are used to SO_2 concentrations up to 10 p.p.m. had no or little effect. According to Haggard, this is due to chronic inflammation of the upper air passages of these people, producing a tenacious mucus which acts as a protective coating. Sulphuric acid in concentrations of 0.35 mg/cm produces the same effect as 1 p.p.m. SO_2.

ably (*e.g.* a pH of 4.8 was found in a patient while suffering from a migraine, this changing to 7.4 the next day and becoming normal again after 2 days, *i.e.* 6.0–6.2), Heinke and Herrmann believe that the acidity correlation is not a direct one, and is caused by the same general weather changes (*e.g.* influx of polar air or cold fronts), which affect both the acidity of the air and the autonomic nervous system.

The skin of patients suffering from eczema has a poor acid regulating mechanism. The skin is often not covered by an acid coating which is a protective layer against bacteria. Alkaline aerosols would counteract this acid balance. These facts may explain, at least partly the curative effects which are observed if eczema patients are sent to high altitudes (see p. 641) or to the sea coast, both areas being characterized by relatively high acidity of the air (Cauer).

CHAPTER 3

Physico-chemical Factors (Aerosols)

by

K. BISA*

(Sect. 4 by S. W. TROMP)

Section 1. Definition of Aerosols

From a physico-chemical point of view the atmosphere can be considered to be an aero-colloidal system, in which very fine solid or fluid particles are dispersed between the gas molecules of the air. A concentration of these particles, both of terrestrial and cosmic origin, in gases are known as *aerosols*. The extensive distribution of these very fine solid and fluid particles in the atmosphere may explain why a truly gaseous atmosphere composed of gases only does not exist.

The properties and distribution of aerosols are determined by the physico-chemical laws of aero-colloids and the various meteorological factors.

As indicated on p. 71, the atmosphere contains a large number of small ions, which are actually composed of clusters of 10–30 molecules, particularly oxygen and hydrogen molecules. The origin of "small ions" has been fully explained on p. 73.

These "small ions" are usually attached to the solid and fluid particles of the atmospheric aerosol and form the secondary ions, of which the largest group is known as Langevin ions. These secondary ions move around as a result of electric fields in the atmosphere. According to the law of Stokes-Millikan, the movements are determined by the size of the particles, the density and the electric charge (both sign and quantity). The number of small ions is closely related to the electric conductivity of the air, the large ions to the electric potential gradient of the atmosphere (see p. 74).

Section 2. Size of Aerosol Particles

The size of naturally or artificially dispersed aerosol particles varies usually

* The present section is a condensed translation of the original German article by K. Bisa. The reader interested in this subject is highly recommended to study the book by H. Nückel (prepared in collaboration with K. Bisa, K. Dirnagl, H. Friebel, H. Martini, J. Albrecht, E. von Wasielewski and G. Worth): *Aerosol-Therapie. Grundlagen und Anwendung,* Friedrich-Karl Schattauer-Verlag, Stuttgart, 1957 (the Editor).

between 2 mμ and 5μ. The latter size corresponds to a mass of 10^{-9} g, which enables the particles to float in the air*. Unless special turbulent conditions prevail, particles above 50 μ are no longer stable.

The lowest boundary of aerosol particles is not very well known because of their usually short period of existence (30 sec or less). In the case of fragments of quartz crystals aerosol particles of 0.5 mμ have been reported. The number of particles varies even more than their sizes. If the average particle content of an atmospheric aerosol is about 10^4 particles of 0.1 μ/cm^3, the aerosol can be considered to be stable. This condition prevails in a dust-free continental air mass. However, air masses are known with more than $4 \cdot 10^6$ particles/cm^3.

Section 3. Physico-chemical Properties of Aerosols

In this section the properties of a single aerosol particle, the velocity of aerosol particles and the physico-chemical processes in aerosol clouds will be briefly discussed.

Properties of the aerosol particles

The relatively small mass of aerosol particles as compared with their surface explains the specific properties of aerosols, in particular the property that the physico-chemical reactions between gaseous fluid and solid phases are considerably accelerated in aerosols.

Due to the second law of thermodynamics, in particular known as the *law of minimum free energy* or *principle of Hamilton,* the fluid or hydrated solid aerosol particles will tend to become globular in shape because the *surface tension* is directly proportional to the surface, which for a constant mass is smallest in a globular body.

The electric charge of the outer surface of aerosol particles is different from the central parts. For example in pure water droplets, the negative surface charge will be present to a depth of $8 \cdot 10^{-7}$ cm, the positive charge goes down as far as $13.3 \cdot 10^{-7}$ cm; in other words an *electrostatic double layer* is formed, in thickness equal to 40 molecules. Due to air turbulence this double layer may be destroyed. The originally electro-neutral particle may obtain a surplus charge either positive or negative. This facilitates the

* The upper size limit of floating particles is a function of the precipitation speed of the particles in the air, which is determined by the formula of Stokes:

$$V = \frac{54.5\ (\varrho_T - \varrho_g) \cdot d^2}{\mu}$$

in which ϱ_T = density of particles in g/cm^3, ϱ_g = density of surrounding gas in g/cm^3, d = diameter of particle in cm, μ = viscosity of the gas in g/cm/sec.

adhesion of new ions with opposite electric charge and causes the space charges in aerosol clouds.

Apart from the surface tension and electric double layer the *vapour pressure* of fluid aerosol particles also plays an important role in the physicochemical behaviour of aerosols. The relationship between vapour pressure and size of particles is indicated by Thomson's formula:

$$Rt \ln \frac{P_r}{P_s} = \frac{2\sigma}{r} V_m$$

in which P_r = vapour pressure of the particle with radius r, P_s = saturation pressure, V_m = molecular volume, σ = surface tension, R = gas constant, t = temperature.

In the atmosphere, *e.g.* in clouds or fog, droplets of different diameter occur, the larger ones of which grow at the expense of the smaller ones. Due to the greater vapour pressure of the small droplets the smaller ones evaporate and after passing the saturation point the fluid condenses on the larger droplets, a process known as *isothermic distillation.* This process is furthered by the surplus charge of aerosol particles, which lower the vapour pressure. These various properties of aerosol particles explain the increased hydration capacity of aerosols with increasing surplus charges of the particles.

Velocity of aerosol particles

The movements of aerosol particles in stagnant air depend on the gravity force, electric forces, etc., and the braking effect caused by the viscosity of the surrounding gas. As indicated above the resulting sedimentation speed

$$V = \frac{54{\cdot}5\ (\rho_T - \rho_G) \cdot d^2}{\mu}$$

in other words the falling speed is directly proportional to the square of the particle size. As a result the smallest particles tend to float continuously. For further details see refs.[223-305] (particularly ref.[285]).

The particle movements as described above are considerably accelerated by air currents. Due to repeated collisions of aerosol particles in air currents the particles increase in size, a process affected by the surplus charges of the aerosol particles.

Section 4. Biological Properties of Aerosols*

by

S. W. TROMP

It is generally known that with decreasing size of particles in an aeroso

* This section is based on the publication by Nückel[285] mentioned above.

cloud, due to the increase in total surface of the particles, the speed of various chemical reactions is accelerated considerably.

As pointed out by Dirnagl 1 ml of water, composed of spherical drops of 1.24 cm diameter, has a total surface of 4.84 cm^2. The same amount of water divided into 523 million droplets of 0.01 mm (or 10 μ) has a total surface of 6000 cm^2. With a particle size of 0.1 μ the number of particles increases to $523 \cdot 10^{12}$, the total surface to 60,000 cm^2.

Goetz demonstrated recently that a certain poisonous gas in the air could be eliminated in 17 h by distributing in the air mass 1 cm^3 of sand particles of 0.1 mm grain size. The same process could be completed in 1 min if a grain size of 0.1 μ is used.

If in a certain microclimate (in buildings or mines) a poisonous gas would be present in a concentration of only 10^{-9} and absorbing aerosol particles of 5 μ are floating in the air, in a concentration of 1 cm^3/m^3 air, the molecules of the poisonous gas will be attached to these particles. The total surface of the aerosol particles of 5 μ grain size amounts to 1 cm^2/l. This surface may be able to absorb about 10^{19} molecules of the poisonous substance. Depending on the size and electric charge of the aerosol particles they are able to penetrate to different levels of the lungs (see later p. 112). However, a concentration of 10^{19} molecules/cm^2 may surpass considerably the threshold of physiological resistance to the poisonous gas. This may explain why even very small concentrations of poisonous substances in fog or industrial aerosols, particularly during atmospheric inversion (see p. 19), may have devastating effects on the lungs of the inhabitants living in such an area. This is also one of the reasons why certain aerosols in coalmining districts with large chemical industries, containing poisonous organic compounds in the air, may be responsible for lung cancer.

The knowledge of the great chemical activity of aerosols has been applied in medicine for more than 100 years, particularly in Germany, France and Italy, in *inhalation therapy,* a name recently changed into the more scientific term of *aerosol therapy*. This method will be explained in more detail on p. 604.

Whereas originally only water sprays in health resorts were recommended, in recent years various drugs are used in aerosol sprays. This is even more successfully applied in low pressure chambers permitting a deeper penetration into the lungs (see later pp. 610 and 633).

Section 5. Radioactive Aerosols

As indicated above, under normal conditions an aerosol particle will have an electrostatic double layer on its outer surface. However, if these particles consist of radioactive substances due to the various radioactive radiations, the double layer is disturbed, affecting the adhesion properties of the particles. It was found that gaseous air polluting substances near industrial centres are able to absorb a considerable number of such radioactive particles owing to these changed adhesion properties of the aerosol.

For certain therapeutic purposes the use of radioactive aerosols has been recommended. Usually radioactive water is used as a spray. According to certain authors the radon (radium emanation) aerosols lower the systolic blood pressure after inhalation and causes a dilatation of peripheral arteries, which seems to afford alleviation to angina pectoris patients. Endocrinal functions are apparently accelerated after radon inhalations. However, these results should be accepted with great caution as many more experiments are required to confirm the reported results.

Recent studies in 1959 by Davis, Logie *et al.*[117] at the University of Texas and at the School of Aviation Medicine at Austin, Texas (U.S.A.) revealed a relationship between natural radioactive pollutants in the air (radon and thoron) and certain meteorological factors. Days with high atmospheric radioactivity were preceded by turbulent winds from the North. This is followed by falling temperature, decreased wind velocity and the formation of an inversion layer. This whole process in Austin is characteristic of cold front passages. Similar relationships were found by Lucas *et al.*[120] in 1957, which suggest that artificial radioactive aerosols after bomb explosions may show a similar meteorologically determined geographical distribution.

CHAPTER 4

Air-polluting Substances

Section 1. Pollution by Organic Particles[306-316]

On p. 96 we discussed the presence of organic "gases" in the atmosphere. In the present section we shall briefly dwell on the distribution of organic "particles".

Three important groups of organic particles are known: pollen, spores and micro-organisms.

1. *Pollen*

Types of pollen

At the time of flowering, many trees and other plants shed great quantities of fertilizing monocellular grains known as pollen. As they play an important role in the causation of allergic diseases, such as hay fever (or pollinosis), a great number of studies on the origin, distribution and toxic contents of pollen have been carried out in various parts of the world (see p. 462).

The plants on earth are usually classified into four large groups: the Thallophyta (comprising Bacteria, Algae, Fungi, etc.), the Bryophyta (or Mosses), the Pteridophyta (or Ferns) and the Spermatophyta (seed plants), the latter being subdivided into Angiospermae (most of the flowering plants and grasses) and Gymnospermae (Taxus varieties, Pine trees, etc.).

Another classification uses the division Cryptogamae (or spore plants) and Phanerogamae (or seed plants). To the first group belong the Thallophyta, Bryophyta and Pteridophyta with spores producing organs, whereas the Phanerogamae contain several pollen-producing plants (*e.g.* grasses) and trees (*e.g.* oak, birch, maple, etc.).

A single birch may produce more than 10 million pollen grains in a season. Pollen is usually very small, as a rule averaging between one hundredth and one tenth of a millimetre. They are, therefore, easily carried by vertical wind currents into higher regions. They may remain there for days, weeks or even months. During this period this *aeroplankton* has usually travelled over hundreds of kilometres. Erdtman[309] was able to collect pollen grains of American plants more than 700 km east of the U.S.A. in the Atlantic Ocean.

The majority of pollen grains consist of 2 coats, an outer coat (the *exine*) and the inner coat (the *intine*). The outer surface of exine is often sculptured or ornamented in some way and this serves for botanical identification.

Time of pollination

The shedding of pollen, known as pollination, depends on a number of factors. The fact that the main pollen season starts about the same period every year (*e.g.* grass pollen begins to flower in the Netherlands every year between 12 and 16 May) suggests that the total solar energy, humidity, etc. received during the preceding months are more important than the immediately preceding meteorological conditions. Obviously these conditions affect the various species of plants differently.

Size of pollen grains

Outstanding pollen- (and hay fever) -producing trees are the maple, oak, birch, poplar, willow, horse-chestnut, elm. The sizes of their pollen grains are 26–29 μ, 26–28 μ, 24–28 μ, 24–26 μ, 14–17 μ, 17–21 μ, 24–28 μ respectively. The pollen grains of grasses vary in size from 22 to 100 μ (p. 463). The smallest grains of plant pollen are usually 10 μ; the largest, 180 μ.

Pollen production

Pohl (*ca.* 1933) studied the pollen output of various plants. This per flower of Gymnospermae, such as *Pinus nigra,* amounts to 1,480,000, of *Picea excelsa* 590,000. Considerably smaller figures are, however, also known, *e.g.*, of the Angiosperm *Acer platanoides* 8,000 (for further details see ref. [309, p. 175]). Calculated/m^2 of soil, the number of pollen grains fluctuate between 100 and 5000 millions. From studies by J. Van Hoorn in 1955, it would seem that the concentrations of grass pollen in the Netherlands in May are 256 pollen per 180 l of air against 10 or less in other periods.

Weight of pollen grains

As they are very hygroscopic, their weight varies with the amount of moisture they contain and that of the environment. The dry weight varies usually between 3 and $75 \cdot 10^{-9}$ g, their volume between 4000 and 140,000 μ^3, their specific gravity between 0.39 and 1.16.

Rate of sinking

In a quiet atmosphere the rate of fall usually fluctuates between 0.9 and 8.0 cm/sec, although much higher rates (up to 40 cm) have been reported. This affects the distribution of pollen little because a vertical air current rising at a speed of only 2 m/sec would reach an altitude of 1800 m in 15 minutes, carrying Larix pollen to 1638 m.

The rate of settling depends closely on the water content of the grains.

Dissemination by air currents

As stated above, pollen grains can be carried hundreds of miles away by air currents. Near Sweden, 30 km off the coast, more than 100,000 pollen were trapped on a boat, making an average of 16 grains/mm^2. Pollen studies in N. Sweden demonstrated the transportation of pollen from S. to N. Sweden, a distance of 1000 km. On the Faeroes the pollen of plants is found growing 420 km away in Scotland. Erdtman[309] collected pollen in the Chatham Islands from plants growing 700 km westward in New Zealand. It has been assumed that winged pollen would travel further than those without wings. However, the advantage of the air sac of winged pollen is offset by the larger size of those grains.

During a sea voyage from Sweden to New York in 1937, Erdtman[309] collected grains of pollen with a vacuum cleaner several times a day. About 18 pollen/m^3 were found in the North Sea, 0.7 in Mid-Ocean, 6.0 near New Foundland, falling to 3.5 near Nova Scotia and rising to 15.0 near New England.

As a rule, the number of pollen in the air is small in W. Europe on quiet days with high barometric pressure; it increases with increasing turbulence and reaches its peak, in particular, during periods of steeply falling barometric pressure.

Pollen counts of the air may vary considerably from one hour to the other. There is usually a peak after sunrise at 7 or 8 a.m. (in the Netherlands), but other high peaks may occur late in the evening or during the night, probably due to turbulent air currents during the night or increased humidity[312]. A fairly striking correlation also exists between the average (and particularly maximum) daily temperature and the total number of pollen, which may become abundant above 15° C. Many meteorological disturbing factors may nonetheless change this pattern.

Recording of pollen

The more simple techniques employ ordinary glass slides placed in the open air. The slides are coated with a thin layer of glycerine jelly which is prepared by soaking gelatine for 2 hours in water and by adding glycerine and carbolic acid[308].

An excellent system for continuous recording was developed by H.A.E. Van Dishoeck (Head of the Department of Otorhinolaryngology at Leiden

University, the Netherlands) in co-operation with J. Van Hoorn. The instrument is a modified slit-sampler of Bourdillon. For 12 minutes of each hour 180 l of air are sucked automatically through the instrument, all particles being caught by a vaseline-coated round disc. Contrary to Bourdillon's technique the slide moves clockwise, 15° every hour, instead of continuously. As a result, 24 lines of pollen (and spores) are automatically obtained on the disc. The pollen and spores are identified and counted under a microscope.

Application of pollen in paleo-biometeorology

Soil samples containing the precipitated pollen grains are analysed and the relative frequency numbers of the different species are compiled in a *pollen spectrum.* This method is known as *pollen analysis.* As pollen spectra indicate specific climatic conditions under which the pollen-producing plants have lived, a series of pollen spectra prepared from samples in a vertical section of soil strata will give us a picture of the climatic and botanical changes thousands or even millions of years ago. The science studying these problems is known as *paleo-biometeorology.*

2. *Spores*

Mechanism of liberation and dissemination

In the higher Fungi (to which belong the Basidiomycetes, *e.g.* Toadstools and Ascomycetes, *e.g.* Moulds) a special part, the *fruit-body,* is concerned with the production and liberation of spores. Although in some species spores are dispersed by flies and rodents, the main factor for dispersion is the wind.

The actual *mechanism of liberation* is clearly described by Ingold[313]. In the group of Hymenomycetes, just before the discharge of the spore, a drop of fluid suddenly appears at the *hilum* (*i.e.* a small projection near the point of attachment of the spore). It grows to a certain size and then the spore is shot away, carrying the drop with it. The distance of discharge in the fungi spores in only 0.005–0.02 cm. There the spores fall in still air in a tube. However, turbulent air currents liberate the spores and carry them high into the atmosphere. Larger fungi specimens (*e.g. Ganoderma applanatum*) are able to produce 20 million spores per minute for 5 or 6 months of their annual activity, which usually begins in W. Europe around May. The discharge goes on even during periods of drought. The fungus *Daldinia* may liberate as many as 10^8 spores overnight, between 9 p.m. and 9 a.m. and only very few during the day. A similar nocturnal rhythm is noted in other fungi. Gregory[312] mentioned the great abundance of hyaline basidiospores of the yeast *Sporobolomyces* during the early hours of the morning (about

7000 m^3), when moist air and dew prevails. The spores are practically absent during the day. Moulds often grow in great profusion under the floors of old, damp houses. On account of their mould spore production they may cause allergic phenomena in people living in those houses. As the dissemination of the spores depends on air currents underneath and through the floors, the number of spores in the bedroom and living-room of such houses and the allergic phenomena caused by them will greatly depend on various meteorological factors such as described on p. 469.

Methods of recording

The methods of recording spores adopted by different research workers vary. We have just described the method used by Van Dishoeck and Van Hoorn for continuous recording. Petri dishes placed in the open air are used in the Asthma Centre at Hilversum (the Netherlands). On the Petri dish there is an aminosol-glucose-agar, acting as the nutrient of the culture. The dishes are incubated for 5 days at room temperature and afterwards the mould colonies are examined under a microscope. Other laboratories use other but similar methods, as described in refs. [311-312]*.

3. *Micro-organisms*

A great number of micro-organisms (both phytological and zoological) are floating in the atmosphere. They represent the *aeroplankton,* which have been described by Gregory[311], Niemann[314,315] and others. The floating movements in still air are determined by their density, size and aerodynamic shape, but in turbulent air the speed of air movement is the dominating factor. Some of the organisms observed in the atmosphere are the following:

(1) *Viruses* (size 10–250 m μ). They may occur in small plant fragments floating in the air or in dust particles. Their dissemination over long distances is very likely in view of the distribution of the heavier spores and pollen in the atmosphere, but so far little research has been done in this very important field.

(2) *Bacteria* (size 0.2–100 μ, mass 10^{-11}–10^{-12} g). More particularly those

* P. H. Gregory was able to demonstrate in wind tunnel experiments (*Nature, 166,* 487 (1950), that the number of spores trapped in a Petri dish depend on particle size, wind speed, dimensions and orientation of the trap surface. The latter can have an overriding effect on deposition. In other words, there is usually no true relation between the actual spore content of the air and the number of spores trapped on the dish. As this type of recording is not continuous, a short rainfall, before the dish is placed outside, may change the number of pollen or spores considerably for a short period. Consequently, values recorded on such a day will not be representative for the whole day.

developed in the protective spore stage (micrococ) after the surrounding fluids are dried up could be transported by air currents over considerable distances and become active again as soon as the environmental conditions are more favourable.

(3) *Algae* (size 1–1000 μ). They have been reported in the aeroplankton of different areas.

(4) *Fungi* (Toadstools and Moulds), *fern* and *moss* spores are common in the aeroplankton. Their sizes vary considerably: 2–100 μ (Fungi), 15–60 μ (Ferns), 10–120 μ (Mosses), etc.

Gregory has pointed out that the presence of micro-organisms in the aeroplankton may not have harmful effects only, such as infectious or allergic diseases, but the daily inhalation of 50 μg of micro-organisms may also have an immunizing effect. The study of these problems is very difficult because of the small mass of these micro-organisms. For microbiological analysis at least a few micrograms are needed, which requires the screening of at least 1000 m^3 of air. As these micro-organisms are surrounded by 10^4–10^6 inanimate particles, which may have inhibiting effects, the situation becomes even more difficult (for further details see Goetz[310]).

The summary given of the distribution of organic air-polluting particles may indicate sufficiently the great importance of this field of study, especially for the analysis of the influence of meteorological factors on the development of allergic diseases such as hay-fever, asthma and certain skin diseases.

Section 2. Pollution by Inorganic Particles[317-327]

The inorganic particles in the air are mainly due to dust composed of soil minerals and fragments from building materials (like cement, etc.). Large amounts of soil minerals are carried into the atmosphere in dry and dusty desert areas in particular, but also in humid climates during hot summers. In the Middle East, this fine dust penetrates through the tiniest cracks near doors and windows, covering the furniture with a thin coating of mineral fragments, at the time of the *khamsin*, when very hot, dry winds prevail. These mineral fragments, because of their crystalline structure, have electrostatic charges which differ for different types of minerals. Experiments by Oppenheim in 1933 have demonstrated the existence of very large *electrostatic charges* on the human body when the atmosphere is very dry. The charges are due to friction between different parts of the body and, particularly, to friction between clothes and the skin and between shoes and the floor. Friction between wool, cotton or silk and the human skin (not the hand) makes the latter usually electrically positive, the clothes being negative. A dressed person is on the whole electrically neutral.

The electric charges are usually several hundred V but in centrally heated, very dry (about 30%) rooms, people walking on rubber shoes may be subjected to charges of 800 V and more on the body. A person dressed in silk sitting on a leather-backed chair and rubbing against it may create several thousand V; against rubber, charges of as much as 14,000 V have been recorded. Similar high electrostatic charges are noticed in motor cars with rubber tyres driving on dry desert soil. A shock is felt if a person sitting in such a car is touched. For this reason special discharge chains are attached to vehicles exposed to these conditions.

Mechanism of penetration of inorganic particles into lungs

Owing to air currents carrying charged mineral particles, these mineral fragments are often attached to our skin or hair. The finest particles, forming electrically charged aerosols, are liable to penetrate into the nose and lungs.

In mines, or in places where excavating or tunnelling takes place, but also in many metal grinding and polishing industries, the penetration of sharp fragments of the minerals quarz, felspar and related silica minerals may cause a dangerous, fibrosis-producing lung disease known as *silicosis*[321,323,326]. It has been estimated, for example, that in 1947 alone between 500,000 and one million people in the U.S.A. were exposed to silicious dusts and that a considerable percentage suffer from silicosis. According tot E.H. Rubin, an X-ray survey in 1930 of 27,533 individuals in the Pilcher district of Oklahoma (U.S.A.) disclosed that 5366 had silicosis. The disease develops after only a few months of strong exposure.

Normally the protective mechanism of the nasopharynx and bronchi is sufficient to keep the lower air passages free from dust, at least as far as mineral particles larger than 10 μ are concerned. More than 75% of particles reaching the alveoli are less than 3 μ (length of the tubercle bacillus). The smaller particles (0.5–3 μ) are the most injurious. Only asbestos dust, as large as 200–400 μ, can slide down the bronchi with damaging effect.

Extensive studies on the penetration depth of aerosols were carried out by the physician Bisa in the Institute of Aerobiology at Grafschaft (Germany) and by the physicist Dirnagl [250-254] at the Balneological Institute of Munich (Germany). As described by Bisa, the specific microclimatic conditions in mines and industries with insufficient air exchange may create electrically charged aerosol clouds. Whereas normally larger dust particles do not reach the lower bronchi, the same, but electrically charged, particles may reach to greater depths.

Mierdel, Seeliger and Straubel [285, p. 20] state that the velocity (in cm/sec) of an aerosol particle is determined by the formula

$$V = \frac{10^{-7} \quad Q \cdot E}{K \cdot d \cdot \upsilon}$$

in which Q = the number of electric charges (1 elem. charge = $1.6 \cdot 10^{-19}$ coulomb), E = electric field surrounding the aerosol (in V/cm), K = frictional constant (in globular particles = 0.69), d = diameter of the particle in μ, υ = viscosity (in g/cm/sec). A particle of 3 μ diameter in a field of 1 V/cm would obtain a velocity of $3 \cdot 10^{-6}$ cm/sec if the electric charge equals one elementary charge. With 1000 elem. charges the velocity is $3 \cdot 10^{-3}$ cm/sec. In other words, the smaller the particles and the higher the charges, the greater the velocity and depth of penetration. Therefore, 90% of an aerosol with many particles of 0.1 μ, each with a great number of elementary charges will remain in the lungs where it is precipitated, against 0.5% if the particles are neutral.

The excess charges, which reach the cells of the lung tissues, are absorbed by the lungs (according to Bisa). The biological effects of this process are further discussed on p. 353.

Summarizing what has been said, the *determining factors in the causation of silicosis* are the fineness and electric charges of the aerosol particles, their concentration in the atmosphere, the percentage of silica minerals and their free silica content, the length of exposure and the presence or absence of lung infections (by streptococci, pneumococci, etc.). The injury does not seem to be caused by the sharpness of the minerals but they seem to induce a fibroblastic reaction in the lymphoid tissue with the formation of nodules. The presence of alkalies apparently accelerates these processes, whereas coal dust, aluminum and other minerals have retarding effects.

Apart from silicosis, other related dust diseases are known, *viz.*, *asbestosis*[320, 327] (near asbest mines), *siderosis*[318] (caused by the inhalation of metallic iron dust in iron mines and iron industries), *anthracosis*[322] (black lungs due to coal dust in mines or due to soot in heavily polluted areas). Whereas these latter three diseases are usually related to local microclimates, only silicosis is a disease which may occur both in local microclimates of mines, etc. and in Middle-East countries with sandy deserts and periods of high atmospheric turbulence. An excellent summary of these various dust diseases is given by G. Worth[285, p. 229–264].

In the following sections P. J. Meade, meteorologist and air-pollution specialist of the Meteorological Office, Air Ministry, London, will discuss in greater detail the mechanisms involved in the distribution of chemical pollutants in the atmosphere, already briefly mentioned on p. 96. In these sections only the direct effect of air-pollution will be discussed.

Possible genetic effects of air pollution

An important aspect is the *possible influence of air; pollution on genetic effects.* Around 1956 interesting studies were carried out by Kotin and Thomas in the Los Angeles area[181]. Extensive research on the possible biological influence of air pollution in low concentration first failed to reveal any consistent, significant results. However, similar experiments with mice in a labile biological state (*e.g.* the conception period or the new born state) demonstrated that a synthetic fog in a climatic chamber in concentrations of 1.25 p.p.m. (produced by gasoline and ozone) significantly reduces the ability of a strain of twelve-week-old black mice to conceive. When conception did occur the litter size was slightly reduced. The effect was most serious on newborn mice, practically all of which died prior to weaning. Kotin's experiments also showed that these effects are primarily due to changes in the female mice, not the male.

It is interesting to refer also to the studies of Bowater and Ford, described by Th. Dobzhansky in his book *Evolution, Genetics and Man* (John Wiley and Sons, Inc., New York, 1955, p. 104). It was found that of the light and dark coloured varieties of the moths *Amphidasis betularia* and *Odontoptera bidentata,* the dark melanic variety has increased considerably in the 20th century in the industrial areas of W. Europe, particularly in England. Originally the light variety was dominant, the dark variety being rare. The two varieties differ only in one single Mendelian gene. However, since the middle of the 19th century dark varieties have increased continuously, particularly near industrial centres. Some populations consist nowadays almost entirely of dark varieties. Ford explains this as follows: he believes that the dark variety is more vigorous than the light one. In non-industrial areas the light varieties would compensate for their different vigour by being protectively coloured. This camouflage would protect them for their enemies. In industrial regions the reverse would take place, the dark ones being better camouflaged.

So far, biologists are inclined to accept this theory as the only explanation. However, further genetic experiments in controlled rooms may show that it is not the colour protection only but the direct or indirect effect of air-pollutants which is responsible for this gradual change in moth population. Further studies on the lung structure of generations of people living in heavily polluted areas may show changes in younger generations of a permanent nature.

Genetic studies in recent years of micro-organisms have shown that, at least in lower organisms, chemical substances seem to be able to create permanent heriditary changes in the physiological properties of these organisms. Evidence for this type of *micro evolution* is the increasing resistance of bacteria (*e.g. Staphylococcus aureus*) to penicillin in successive generations, of the housefly (*Musca domestica*) to D.D.T. sprays and so forth. Although part of this phenomenon of adaptation can be explained by the death of less resistant forms in the first generations and a natural selection of stronger species, it is doubtful whether this applies to later generations which can resist concentrations of a poison which would have killed all the organisms, without exception, if applied in the same concentration in the first generation.

It is fully realized that the points raised are rather speculative, but they have been raised intentionally because it appears as though hitherto the study of the possible genetic effects of air pollutants has been confined to radioactive aerosols.

Section 3. Chemical Pollutants[328–343]

by

P. J. MEADE

1. *General Classification*

In turning now to our final classification, chemical pollutants, we are concerned mainly with the impurities released to the atmosphere as a consequence of mankind's industrial activity. An exhaustive list based on present knowledge would be very large and would have no sure claim to completeness. In a highly industrialized country like the U.S.A. more than 100 pollutants have been identified and perhaps many others remain undetected while still more may be added as variations or developments occur in existing methods of fuel consumption. Fortunately it is possible to consider the great majority of chemical pollutants by means of a small number of categories as Table 17 indicates.

TABLE 17

CHEMICAL POLLUTANTS IN THE ATMOSPHERE

Category	*Examples*
Small particles	smoke, ash, grit
Sulphur gases	SO_2, SO_3, H_2S
Nitrogen gases	NO, NO_2, NH_3
Ozone and oxides of carbon	O_3, CO, CO_2
Halogens	HF, HCl
Radioactive matter	^{41}A, ^{131}I, particles

The major sources of the categories of pollutant mentioned in this table are the burning of fuel and chemical works and, in the case of radioactivity, there are natural sources as well as those resulting from weapon tests and from the operation of nuclear reactors in the peaceful uses of atomic energy.

When coal and oils are completely burned with air the principal gaseous products entering the chimney stack are carbon dioxide, nitrogen, sulphur dioxide, excess air and water vapour. With coal most of the mineral matter is usually left as clinker or ash, though a proportion, depending on the type and grade of fuel and on the conditions of firing, is carried forward as dust or grit with the chimney gases. If combustion of coal or oil is incomplete, the products include not only those already mentioned but also carbon monoxide, hydrocarbons and other gases, and also smoke in the form of soot and tarry matter. Gas made from coal for public supply is generally purified before distribution and freed from all particles of tar and nearly all of the sulphur compounds; on complete combustion carbon dioxide is formed together with water vapour but only very small quantities of the sulphur oxides are liberated.

Table 18, taken from the Report of an official Committee on Air Pollution[329], gives the principal uses of fuels and estimates of pollutants discharged in Great Britain during the year 1953. In other countries the sulphur content of indigenous coal may differ from that mined in Great Britain but otherwise this table may serve as a typical example of the gross pollution released to the atmosphere in a country with a high rate of industrial activity.

The output of noxious gases from chemical works and similar plants is, in most countries, carefully controlled by legislation, for example, in Great Britain by means of a series of Alkali Acts and Public Health Acts. In many of these industrial plants the waste gases which result from the primary processes are by no means valueless and this consideration greatly assists the enforcement of legislation. The gases which, in the absence of recovery measures, could be released include hydrochloric acid, hydrogen sulphide, sulphur oxides, the oxides of nitrogen, ammonia, chlorine, hydrogen fluoride and many others. These gases could all be very harmful in their various ways but fortunately, in addition to their potential value as by-products, they are fairly easily recovered and the quantities reaching the atmosphere do not at present constitute a grave problem except perhaps under rather localized conditions. Cholak[330] has presented data on the pollutants present in the atmosphere of a number of communities in the U.S.A. and Table 19 shows the average concentrations (in p.p. 100 m.) of various gases.

From this table it can be seen that the oxides of nitrogen can be present in

TABLE 18

MAIN USES OF FUELS AND ESTIMATES OF POLLUTANTS DISCHARGED GREAT BRITAIN, 1953

Class of consumer	*Fuel supplied*	*Fuel burned*			*Pollutants discharged*		
		solid	*liquid*	*coke oven gas*	*smoke*	*grit and dust*	SO_2
	million tons	*million tons*	*million tons*	*million ft.*^{3}	*mill. tons*	*mill. tons*	*mill. tons*
Coal							
Domestic	36.8	36.8	—	—	0.9	0.1	0.9
Electricity works	36.7	36.7	—	—	small	0.3	1.0
Railways	13.8	13.8	—	—	0.3	0.1	0.4
Industrial, etc.	64.6	64.6	—	—	0.8	0.3	0.1
Coke ovens	25.9	—	—	73,976	small	small	0.1
Gas works	27.2	6.2	—	128,040	small	small	0.2
	205.0						
Coke (excluding gas works and blast furnaces)	—	14.7	—	—	nil	small	0.4
Oil							
Diesel and gas oil	3.0	—	3.0	—	—	nil	0.1
Fuel oil	5.3	—	5.3	—	—	nil	0.3
Creosote-pitch mixture	0.7	—	0.7	—	—	nil	small
	9.0						
Total		172.8	9.0	202,016	2.0	0.8	5.2

TABLE 19

MEAN CONCENTRATION OF POLLUTANTS IN CERTAIN INDUSTRIAL LOCALITIES IN U.S.A. (IN p.p. 100 m.)

Community	*Oxides of nitrogen*	*Chlorides*	*Ammonia*	*Fluoride*	*Oxides of sulphur*
Baltimore	26	3.7	1.8	1.8	7.4
Cincinnati	23	3.3	2.3	0.5	6.4
Donora	15	7.1	—	0.6	1.5
Los Angeles	10	—	—	0.8	5.0–20.0

the atmosphere of some communities in greater quantities even than sulphur dioxide. The nitrogen compounds result from the manufacture of nitric and sulphuric acid and from many other processes. Moreover the exhaust gases of vehicles contain appreciable amounts of the oxides of nitrogen and also of carbon monoxide. The latter is caused by incomplete combustion of fuel in internal combustion engines and the highest concentrations are found in busy streets and in transport garages. Carbon dioxide is one of the permanent constituents of the (unpolluted) atmosphere but this gas must be regarded as a pollutant because many tons of it are discharged to the air every day in towns where fuel is consumed on a large scale, whether in factory processes or in automobiles. In some industrial areas[330], the amount of carbon dioxide introduced artificially to the atmosphere may be equal to the amount occurring naturally in the air, but even so the concentrations are not dangerous to man.

Ozone is a gaseous contaminant which has become well known, chiefly in connection with the smog problem in Los Angeles. Haagen-Smit[334] found that a considerable increase in the concentrations of ozone occurred in daylight during smog conditions (see p. 90) and suggested that the ozone was formed photochemically by the action of sunlight upon the impurities, such as hydrocarbons and aldehydes, already present in the air. The smog problem in Los Angeles is in many ways unique and is associated with an unusual but persistent set of meteorological conditions (see p. 19).

The dangers of radioactivity in the atmosphere form a comparatively modern problem in the public mind but throughout history the environment of man has contained small, variable amounts of ionizing radiation. Recent years, however, have seen the addition of similar radiations as a result of nuclear weapon tests and of certain industrial usages and processes. Radioactivity cannot be reduced by any known process and, in fact, time is the only significant decaying factor.

The main sources of natural radioactivity are the residual amounts of cosmic radiation, which originates in outer space and is largely absorbed in the atmosphere before reaching the surface of the earth, and the elements uranium and thorium which are universally distributed in trace quantities in rocks and soils. These two elements disintegrate into daughter products, *e.g.*, radon and thoron, which are themselves radioactive.

The level of natural radioactivity is small and has been estimated[341] as a dosage to the individual of about 0.1 roentgen/annum compared with a maximum permissible dose, as recommended by the International Commission on Radiological Protection, of 0.3 roentgen/week. Nevertheless, natural levels must be taken into account in considering the effects likely to result from developments in the industrial and other uses of radioactivity. When a nuclear reactor or a radiochemical processing plant is brought into operation there is a risk of release, if not an actual release, of radioactive material to the atmosphere. This release may take the form of a gas or vapour or very small particles, and it may be continuous, as a result of routine operations, or of limited but excessive occurrence, as may be the consequence if an accident occurs.

The source of released radioactivity may be of several kinds. In the simplest case, that of an air-cooled reactor, the source is the chemically inert gas ^{41}Argon. In radiochemical processing plants, the effluent contains isotopes, such as ^{131}Iodine, which react with vegetation and may endanger health if absorbed into the human system. Particulate effluents also present special problems which are chiefly associated with deposition upon surfaces or vegetation.

2. *The Measurement of Air Pollution*

Pollution of the atmosphere is an important social problem but before any action can be taken to remedy this evil it is usually essential in the first place to demonstrate the presence of contaminants and secondly to assess the extent of the nuisance or damage. The subject is best dealt with on a national scale but the detailed study of pollution is essentially a local problem. In any area the atmospheric pollution is made up of two components, a *background* pollution attributable to distant sources and a *local* pollution caused by the fuel consumption and general industrial activities in the area itself and in the immediate neighbourhood. For example, a country district with few houses and remote from any industry, will usually have a small but measurable amount of pollution in its atmosphere. Similarly, an industrial area, with perhaps a high level of pollution, would not be entirely freed from it if all the industries and domestic fires in the locality ceased to function. These considerations have been stressed in a study by Meade and Pasquill[340] of the distribution of pollution in a country area in which an isolated source of pollution had been established. They were able to separate the average pollution into a background contribution and one arising from the local source.

For a quantitative examination of air pollution it is necessary to have available efficient sampling and measuring techniques and much progress has been made over the past few decades in meeting these requirements. Even so there is much still to be learned about the separate constituents of polluted air and about the chemical and other processes which occur. A very full description of sampling and analysis procedures may be found in the *Air Pollution Handbook*[339] and the subject has also been treated extensively by Meetham[342]. It will therefore be sufficient in this book to refer briefly to some of the more commonly used instruments and techniques.

3. Smoke Measurement

A simple but very practical means of smoke measurement which is used in many countries is the Ringelmann shade chart. The density of smoke is estimated by comparing the shade of the smoke with a series of cards held about 15–20 yards from the observer and preferably in line with the chimney producing the smoke. The cards are white with black horizontal and vertical lines superimposed so that increasing density on the scale is indicated by thicker and thicker lines, *i.e.*, by a greater area covered black on a card. The cards give a "Ringelmann number" of smoke density according to the following scheme (Table 20). Urban regulations usually impose a time limit, about 2 or 3 minutes, during which any chimney is permitted to discharge smoke of density Ringelmann 2 or worse continuously.

TABLE 20

SCHEME OF RINGELMANN NUMBERS OF SMOKE DENSITY

Number	*Area of card shaded black*	*Description of smoke*
0	0%	no smoke
1	20%	light grey
2	40%	darker grey
3	60%	very dark grey
4	80%	black
5	100%	dense black

The concentration of smoke in the air near ground level can be measured by drawing a known volume of air through filter paper which will intercept and retain almost all the particulate matter in the air. The average concentration of the smoke is then estimated by matching the stain on the filter paper with a standard set of shades calibrated against an equivalent volume of air. As a rule filters are changed every 24 hours, thus giving an average daily concentration, but the diurnal variations in smoke can also be estimated by changing the filter paper every 1 or 2 hours and comparing with a set of shades corresponding to the volume of air drawn through the filter papers. Concentrations measured in this way can be expressed according to shade numbers or their equivalents in mg/m^3.

4. Measurement of Deposited Particles

Tar, grit and other particles which are eventually removed from the air by deposition can be detected by exposing a sheet of adhesive paper or glass.

However, to obtain quantities which can be weighed reasonably accurately a long period of exposure is necessary and a deposit gauge is then used and placed in open surroundings so that the results obtained may be regarded as representative of the neighbourhood. The deposit gauge is similar in many respects to the traditional instrument for the measurement of rainfall, that is, a collecting funnel of about 1 ft. diameter leads into a glass collecting jar large enough to hold all the rainfall as well as the deposited matter collected during the period of exposure, which is usually one month. Various precautions are taken to exclude leaves and other unwanted substances and to prevent chemical reactions in the jar.

The material collected in the deposit gauge is measured under the broad headings "water soluble" and "water insoluble" deposits and expressed as tons/mile^2/month. More refined analyses can, however, and frequently are made in order to determine the amounts of tar, ash, calcium, chloride and sulphate, etc., that have been deposited.

5. *Measurement of Sulphur Dioxide*

As a gas, sulphur dioxide (see pp. 96 and 499) is not deposited in the same way as ash and cannot be intercepted by a filter paper like smoke. Chemical techniques must therefore be employed to determine the quantity of sulphur dioxide present in a sample of air. A volumetric method, commonly combined with the filter paper technique for estimating smoke, consists of passing a known volume of air through a dilute solution of hydrogen peroxide. Any sulphur dioxide present in the air is removed in accordance with the reaction

$$H_2O_2 + SO_2 \rightarrow H_2SO_4$$

From the state of the liquid before and after sampling, the amount of sulphur dioxide in the volume of air is readily calculated and this is expressed in p.p. 100 m. of air.

Volumetric systems can, of course, be applied to the measurement of other impurities than sulphur dioxide, *e.g.*, aldehydes, ozone, chlorine, ammonia.

A standard method in use in Great Britain for determining the quantity of sulphur dioxide in the air is based on the fact that this gas reacts slowly and uniformly with lead peroxide to form lead sulphate

$$Pb\,O_2 + SO_2 \rightarrow Pb\,SO_4$$

What is measured therefore is the rate of sulphation over a period of a month of a cylinder coated with lead peroxide. The cylinder is placed in a louvred screen, similar in concept to that used for the measurement of air temperature, and by this means protection from rain is obtained while the air is able to flow freely.

6. *Measurement of Atmospheric Radioactivity*

The measurement of the radioactivity of the air is mainly concerned with (*i*) natural radioactivity, (*ii*) particulate fission products in the air and (*iii*) deposition from the air of particulate fission products.

The techniques of sampling for subsequent analysis are, in principle, similar to those in use for the collection of smoke and ash. For (*i*) and (*ii*), known volumes of air are drawn through a special filter, a suitable example being Whatman paper[331], which has a very high collection efficiency for particles greater in size than 0.1 μ. For (*iii*), rainwater is collected in a special container made of such materials as polythene or stainless steel which do not alter the isotopic or radiochemical composition of the sample.

While the sampling techniques follow traditional lines, the methods of analysis are highly specialized and account has to be taken of radioactive decay times and, where disintegrations into daughter products occur, analyses should be made when equilibrium exists between parent and daughters. Facilities for such complex procedures are not at present widely available and this is a problem which will call for extensive organisation if a large network of stations for the measurement of radioactivity in the air is to come into being.

Section 4. Physical Principles involved in Atmospheric Diffusion of Pollutants[344-352]

by

P. J. MEADE

The impurities discharged into the atmosphere are for the most part gases or minute particles with only small or negligible falling velocities. In this description are included not only the smoke and gaseous effluent from chimneys but also the particulate clouds of insecticides released as sprays for agricultural purposes and the airborne pollens and spores which are generally called aeroallergens because of the reactions they produce in sensitive individuals. When these impurities enter the atmosphere the principal factors controlling their subsequent history are meteorological processes, of which the most important is atmospheric diffusicn. Meteorology is by definition the physics of the atmosphere and it is therefore appropriate to discuss the main physical principles involved in atmospheric diffusion before describing in the next section the more practical subject of the effects which are produced on pollutants in the atmosphere by highly variable meteorological factors.

In problems of air pollution we are concerned chiefly with the lowest few hundred feet of the atmosphere and the physical properties of importance are those associated with the wind and its turbulence, the variation with temperature in the vertical, the scavenging effects of rain and the influence of fog.

Wind and turbulence

The motion of the air which we call wind is caused by differences in pressure from one place to another and by the earth's rotation in space every 24 hours. The forces resulting from these effects produce a mean wind such as when we say the wind is blowing from the West at a speed of 10 knots. However, a mean wind is more of a convenient definition than a physical reality since, as we would find by reference to an anemometer which measures wind speed and direction, the actual wind fluctuates rapidly in gusts and lulls about a mean value which is not by any means constant. The point can be further illustrated by observational experience. For example, anyone who has looked at a field of corn in a moderate breeze must have noticed the upper surface of the corn rising and falling as if being swept over by waves which, however, reveal no obvious regularity in their pattern. Fig. 20 shows a typical anemometer record from which it

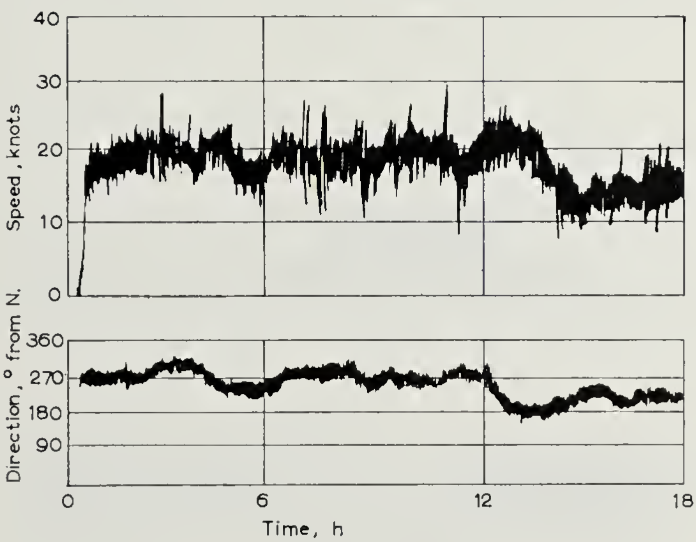

Fig. 20.
A typical anemometer record.

can be seen that both the speed and direction of the wind are subject to oscillations of varying amplitude and period.

Thus, the motion of the air is highly irregular or, in technical language, turbulent and the irregularities or turbulent fluctuations about the mean wind are produced by eddies which may cover a very great range in both size and frequency. Generally it will be found that for any particular locality the turbulence is greatest when the wind is strongest.

Since in atmospheric pollution problems we are concerned with the layer of air near the ground, we must also take into account the fact that the turbulence or gustiness of the wind is affected by the type of terrain over which the air is moving and the obstacles presented to the free flow by means of hills, trees, buildings and so on. When the ground is rough compared with (say) a field where the grass is mown frequently, the frictional drag of the earth's surface on the air moving over it is large and induces in the air a greater intensity of turbulence than would otherwise be present. An aggregate of obstacles such as a wood or a building site may be regarded as having the effect of extremely rough terrain while isolated obstacles such as a tree or a tall chimney are also important because they give rise to eddies on their lee or sheltered side which may give the air with its embedded impurities a downward component of motion.

Major variations in topography as in the case of hills or valleys may also increase turbulence but their principal effect is to divert the general air stream, *e.g.*, channelling between two hills or forcing the air upwards or inducing the air to flow downwards. Fig. 21 shows, in a schematic way,

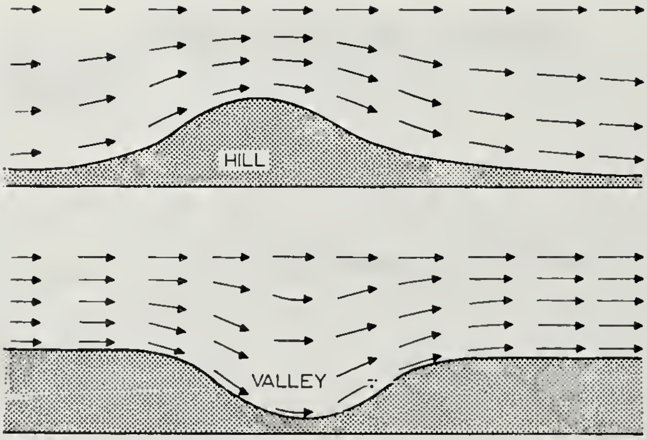

Fig. 21.
Effect of hill or valley on air flow (schematic).

how a hill and a valley may affect the air flow when the wind is directed towards them.

So far all that has been said has referred, at least by implication, to winds blowing horizontally but it should be made clear that the air may also have a vertical component of motion and that this will be turbulent. As a general rule, except in large convection currents as with thunderstorm clouds, the vertical velocity of the air is many times less than its horizontal speed but such motion, whether downward or upward, is of great importance.

In the air pollution problem the wind and its turbulence are major factors because they are the agents for the transport and mixing of impurities in the atmosphere. Transport is effected by the mean wind while mixing is brought about by turbulence or eddies. Turbulence is essentially a large-scale mixing process and this incessant stirring up of the air near the ground has had a profound effect on the development of life on the earth. The scattering of seeds and pollen, the evaporation of water and its distribution far and wide as vapour and then as rainfall are the results of turbulence. As Sutton[352] has said, without this automatic means of mixing in the atmosphere, man could not live in large communities—he would be poisoned by his own by-products. Without turbulence, the smoke from domestic chimneys would accumulate around the roof tops and streets would be filled with the exhaust fumes from vehicles. Fortunately the atmosphere is nearly always sufficiently turbulent to cause rapid mixing which moves effluent plumes sideways and vertically at the same time diluting them with air so that initially dense concentrations of pollutants are eventually scattered throughout an enormous volume of the atmosphere. On occasion, however, the dispersive power of the atmosphere is greatly reduced and when this happens the possibility of heavy concentrations occurring near ground level may be very much increased. In common with its other properties, the atmosphere's efficiency as a mixing agent is highly variable. As already explained, the degree of turbulence varies with the wind strength but these two factors, besides being related to each other, are also affected by another meteorological parameter, the vertical distribution of temperature.

The variation of temperature with height

In the normal course of events the temperature decreases with height from the surface up to the base of the stratosphere but this is not always the case and sometimes in a shallow or a deep layer there may in fact be an increase of temperature with height, in other words, a positive temperature gradient. Such a layer, when it occurs, may be the one adjacent to the ground but occasionally it may be an isolated layer with its base a few hundred feet or even several thousand feet above the earth's surface.

The vertical temperature distribution is largely a question of radiation in which the sun, the earth and clouds have all an important role. The air itself, excluding clouds, is not a good radiator or absorber of heat and is concerned in the process of exchanges of heat energy by means of conduction. On a clear, calm day the ground is heated by the sun's rays to a temperature well above that of the overlying air. The ground radiates its heat almost as a black body and at the same time warms slightly by conduction a thin layer of air immediately adjacent to it. Equilibrium between the incoming radiation from the sun and that emitted by the earth is reached about an hour or two after midday and thereafter, on balance, the earth loses more heat than it gains from the sun and its temperature falls. At sunset, the main source of incoming radiation is cut off while the ground continues to radiate and in consequence cools more rapidly, at the same time cooling the air just above it. This process continues until shortly after sunrise when once again the ground is a net gainer of radiation and its temperature rises.Thus the daily cycle of temperature changes is such that the ground and the air next to it are warmest some time after midday and coldest about dawn, as illustrated in Fig. 22. The air above the surface layer is comparatively unaffected by these radiation exchanges since conduction of heat by air is a slow process. During the major part of the day, therefore, the temperature of the air decreases with height, a condition known as "lapse" or "unstable" and during the night the temperature increases with height and this corresponds to an "inversion" of the normal gradient in the vertical, implying atmospheric stability. The changeover from lapse to inversion and *vice versa* are marked by short transition periods of zero or "neutral" temperature gradient.

In accordance with the laws of physics, warm air is less dense than cold air. Hence in lapse conditions there is light air below and heavy air above and the situation is one of instability. Inevitably convection currents are set up, with the result that turbulence or mixing power is increased. On the other hand, during inversion conditions colder and therefore heavier air is below warmer air, there is little tendency for upward currents to form and so turbulence is suppressed and may die out altogether. The transition period, with the atmosphere neutral, corresponds to an average degree of turbulence.

The discussion so far has been concerned with calm, clear weather and it is in such circumstances that the effects of night inversions and day-time lapses are most strongly marked. In conditions of cloud and wind these effects are reduced and may even be damped out altogether when the sky is overcast with a strong wind blowing. Fig. 22 shows for a typica inland station[348] the differences between the diurnal curves of temperature on clear and overcast days in summer, when the sun's rays are most effective, and in winter. Cloud is a good radiator and absorber at terrestrial temperatures and intervenes in an important way in the transmission of energy from the sun to the earth and the return flow from the earth to the outer atmosphere. When the sky is overcast, therefore, much of the sun's radiation is absorbed before it can reach the ground and, in consequence, the day-time rise in temperature is reduced. At night the radiation from the ground is absorbed by the sheet of cloud and some of it is re-radiated downwards so that the cooling of the earth's surface proceeds at a much slower rate.

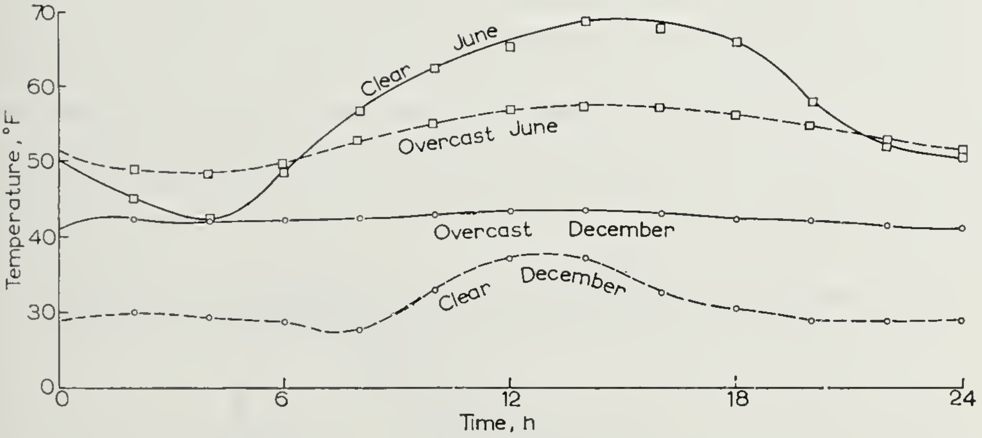

Fig. 22.
The diurnal variation of temperature on clear and overeast days in June and December.

Strong winds which, as we have seen, are very turbulent also act towards the equalization of temperatures but their effects are mechanical, by contrast with cloud sheets which modify the radiation process. When a strong wind is blowing, the air nearest to the ground is constantly changing because of the mixing that goes on and no separate portion of the atmosphere has time to acquire much heat from the earth by day or to supply much by night through the effects of conduction.

In combination, strong winds and a overcast sky maintain zero or very slight temperature gradients until either the wind falls off or the clouds break. The influence of the wind on the vertical temperature distribution is to some extent reversible. While strong winds help towards uniformity of temperature, an inversion denotes atmospheric stability and has a strong tendency to reduce the speed of the wind both in the horizontal and in the vertical.

To sum up the effects of the inter-related factors—wind, turbulence and temperature gradient—it can be said that the turbulence of the natural wind and its speed determine the size and shape of the volume of air within which an effluent plume is diffused and thereby affects the concentration of pollutant at various distances from the source. In lapse or unstable conditions diffusion is rapid and the cross-wind dimensions of the plume show big increases downwind but "looping" of the plume as a whole also occurs with the larger eddies bringing its path quite close to the ground at distances not far removed from the stack. When the atmosphere is in neutral equilibrium the diffusion conditions are much steadier, the axis of the plume maintains its path downwind and the lateral and vertical spread increase fairly smoothly. Under inversion conditions vertical mixing is noticeably restricted and, in consequence, the lower boundary of the plume may not reach ground level for some considerable distance downwind. The atmosphere, however, does not always conform to just one equilibrium condition since discontinuities of temperature gradient in the vertical are frequent. There are numerous possibilities, such as a neutral layer beneath an inversion or an inversion below an unstable layer, and all the combinations as they occur must be considered in relation to the height of the chimney and to their probable effects on the buoyancy and momentum of the emergent plume.

Anticyclonic inversions

In the preceding paragraphs the formation of air inversion by radiation processes was described. There is, however, another type of inversion which, because of its persistence, is also of very great importance in air pollution. This type is experienced mainly during the winter months in periods of quiet, anticyclonic weather and is formed by the slow subsidence of air from a higher to a lower level in the atmosphere. For that reason the term "subsidence inversion" is frequently applied to this category.

In the atmosphere the pressure, as is well known, decreases with height and so subsiding air moves into a region of increasing pressure. In doing so, compression takes place and as the process is adiabatic, *i.e.,* no gain or loss of heat, the temperature of the descending air must rise. The outcome of the subsidence is therefore the establishment of an inversion not at the surface but at some such height as 500 ft., 1000 ft. or perhaps 2000 ft. An inversion of this type in winter may persist in one region for several days and its importance arises from the fact that it may act as a lid preventing the escape of the pollution released to the atmosphere from all the chimneys in the region. The notorious London smog of December 1952 (ref.[344]), which has been blamed for over 4000 deaths, occurred during an anticyclonic inversion lasting for nearly 5 days. This event is discussed more fully on p. 499.

Diffusion accompanied by deposition

If any portion of the gross atmospheric pollution is in the form of grit or particles, the possibility must be considered that sedimentation or deposition on to the ground or buildings may occur. In other words the grit or particles may be sufficiently large, *e.g.*, greater than about 1μ in diameter, to acquire a significant falling velocity and eventually leave the atmosphere. The presence of a "sink", as this effect may be termed, renders the diffusion problem more complicated, since the strength of a source emitting pollutants can no longer be regarded as a constant and some attempt must be made to take account of the depletion of airborne material with distance travelled. If the particle size distribution of pollutants at the source is known, the problem becomes more straightforward and to some extent diffusion and deposition can be considered separately. Fig. 23, which is taken from a paper by Hawkins and Nonhebel[347], illustrates the application of this principle.

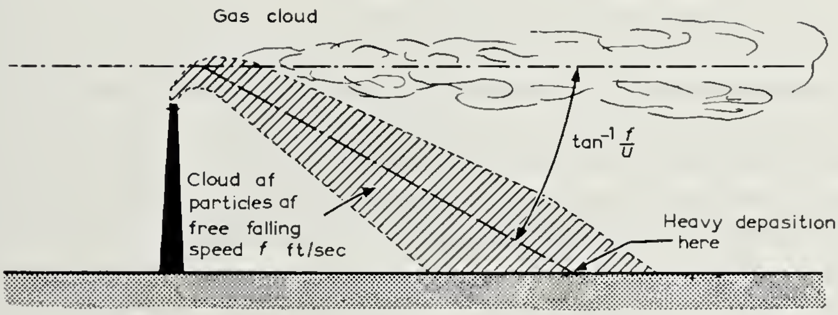

Fig. 23.
Dust clouds and gas clouds. Wind speed = u ft./sec.

The area defined by diagonal lines indicates the process of deposition of the heavier particles while the lighter particles are transported downwind within the boundaries labelled gas cloud. If the horizontal wind speed is u ft./sec, then the trajectory of a particle falling vertically with a velocity f ft./sec makes with the horizontal an angle whose tangent is f/u.

Deposition of pollutants has been treated by several writers, notably by Bosanquet *et al.*[345] and by Johnstone and Roberts[349], and has assumed greater importance in connection with man-made atmospheric radioactivity. Some of the isotopes of this form of radioactivity may react with vegetation or otherwise become liable to enter the human system and the results, to say the least, may be a considerable threat to health. Chamberlain[346] has discussed theoretically the deposition of radioactive particulate matter.

Scavenging effects of rain

It is an accepted fact of experience that the air after a shower of rain feels much cleaner and is seen to be much clearer because of the improvement in visibility that occurs. Precipitation is effective in scavenging or washing-out particulate matter from the atmosphere over its whole depth from the surface up to the level inside the cloud where the rain elements are forming most actively. Our knowledge of the mechanism of the scavenging process is somewhat incomplete but, as Langmuir[350] has shown, a raindrop falling through an aggregate of particles will collect a fraction of those in its path. The collection efficiency of the drop depends on the rates of fall of the drop and the particles, *i.e.*, on their sizes. Raindrops cover a wide range of sizes so there will be variations in the effectiveness of scavenging according to the type of precipitation. For that reason showers which produce the largest drops are noticeably more efficient in cleaning the air than ordinary rain.

Some atmospheric impurities, especially certain gases, may react chemically when they come into contact with raindrops and are then removed from the atmosphere by a chemical rather than the physical process described in the preceding paragraph. A common example is provided by sulphur dioxide which combines with water to form the rather weak sulphurous acid which is nevertheless harmful when it is brought by rain into contact with exposed surfaces, such as the paintwork on buildings. For a detailed account of chemical reactions in the atmosphere, the *Handbook of Air Pollution*[351] should be consulted.

Influence of fog

Everyone is familiar with the fact that fog is much more unpleasant in an industrial and densely populated area than in remote country districts. The reason for this contrast is that in a town the fogs are laden with pollutants and are therefore dirty, whereas in rural areas only pure water fogs occur as a rule. Fog and pollution react upon each other and as far back as 1905 a notable apostle of clean air, Des Voeux, coined the word "smog" to describe the unpleasant phenomenon of fog in association with smoke.

There are several types of fog but one physical process, cooling, accounts largely for their formation. The most important type, radiation fog, results in certain conditions from the cooling of the earth at night when the sky is clear (see page 54). As the air next to the ground cools an inversion is formed and this makes the air stable so that mixing or turbulence is reduced. As cooling continues, the temperature of the air may reach or fall below its its dewpoint and then condensation into fog droplets begins. However, it is not sufficient for the air to become saturated; an adequate supply of nuclei with an affinity for water must be available before the formation of fog can take place to any appreciable extent. It so happens that there are usually sufficient of these so-called hygroscopic nuclei present in the air, for example, minute salt particles blown into the air by sea spray, for fog to form when sufficient cooling has occurred and also, an important condition, provided there is a slight wind to cause a small degree of mixing in order to give the fog depth. In the total absence of wind the condensed moisture in the lowest few inches of air may be deposited as dew.

Some impurities are able to serve as hygroscopic nuclei and one of the consequences of pollution in a fog is to increase the number of droplets that are formed. The fog, therefore, is more dense than would otherwise be the case and, with the other non-hygroscopic impurities such as ash in suspension, the fog becomes dirty. Moreover, since the conditions which lead to the formation of radiation fog are similar to those which produce inversions and prevent the rapid dispersal of pollution, the concentration of smoke and other impurities is likely to be abnormally high in times of fog.

A tendency has been observed for pollutants, whether attached to water droplets or merely suspended in a fog, to fall out very slowly to the ground. Such a fog remains dirty, however, because the output of pollution is a fairly continuous process but there can be little doubt that fogs would be much cleaner if the consumption of fuel could be reduced considerably when the meteorological conditions favour the onset of fog. Alternatively, if the consumption of fuel in domestic houses, which emit pollutants at a low level, could be stopped whenever a fog formed, the fog would become much cleaner within a few hours.

Impurities suspended in a fog have another indirect, but important, effect on atmospheric diffusion. This is concerned with radiation. A fog usually clears in the daytime because a portion of the energy incoming from the sun is able to penetrate the fog and heat the earth's surface. As a result, convection currents can be set up and also the air may be heated to a temperature above its dew point. Both these effects, either separately or in combination, can disperse a fog but the basic requirement in quiet weather is that the ground should be heated. Now the sun's rays can pass through a pure water fog much more easily than through a dirty fog laden with pollution. The reason is that the suspended impurities help to cut off the sun's radiation, in some cases absorbing it and in others reflecting it. A fog in a town with a high pollution level is, therefore, much slower to clear than a fog in open country, perhaps only a few miles away. Thus, in consequence of this rather indirect radiation effect, turbulence is set up earlier in a rural area than in a town although the latter may have a more urgent need.

Section 5. The Effects of Meteorological Factors on Atmospheric Diffusion of Pollutants[353-364]

by

P. J. MEADE

The meteorologist tries to apply the laws of physics in studying problems of the atmosphere and in the preceding section we have seen how a variety of physical principles are important factors in atmospheric diffusion. By considering the subject primarily from the standpoint of physics we were able to form a somewhat qualitative picture of the mechanisms which made up diffusion in the atmosphere. In this section our objective is to go forward from the physical basis to an assessment of the effects produced by meteorological factors, and in so doing, we aim at a quantitative appreciation of the history of pollution when subject to the process of atmospheric diffusion. It should be mentioned that the subject is an extremely difficult one, full of uncertainties, and nothing approaching an exact treatment is ever likely to be possible. Because of its importance, much theoretical work has been done on diffusion and the mathematical theory developed by Sutton[364] has been found to give satisfactory results when applied to the travel of a smoke plume over moderate distances during average meteorological conditions. Sutton's theory provides the basis for what follows.

Observations of concentration over a network of well-exposed, representative points are among the first requirements for a quantitative survey of air pollution. Measuring instruments have already been discussed in Section 3, but here we wish to refer to an important aspect, the time over which an observation is made. The sampling time, as it is called, must be carefully considered because, however accurate and discriminating the instruments in use, there must always be a number of uncertainties due to variations in weather conditions, the type of terrain, the presence of obstacles, etc., in regard to the quality of the sample of air obtained for analysis. When smoke emerges from a source and travels with the wind, the width of the plume increases with distance from the source. If the mean direction of the wind is steady and if samples of the cloud are taken on and at right angles to its axis at some distance downwind, it would almost invariably be found that the concentration is a maximum on the axis and falls off quite regularly on each side. If the values are plotted on a graph, a concentration curve could be drawn and it would be seen to resemble a Gaussian error curve. The shape of this curve depends upon the time of sampling in a manner illustrated in Fig. 24 which is based on the argument put forward by Sutton[364]. If the time of sampling is short, perhaps a few seconds, then the concentration curve has a high peak and falls off rapidly on each side of the axis. On the other hand, a fairly long period of sampling, exceeding 10 minutes or so, results in a wider curve of concentration with a lower peak or maximum value. Of the two types of curve, the one with the longer sampling time is to be preferred, since it incorporates the effects of eddies of all sides and thus provides a realistic picture of the results of diffusion. The short period or "instantaneous" sample is inevitably of a restricted type and should only be compared with other instantaneous samples, but even then the results may not be of much practical value.

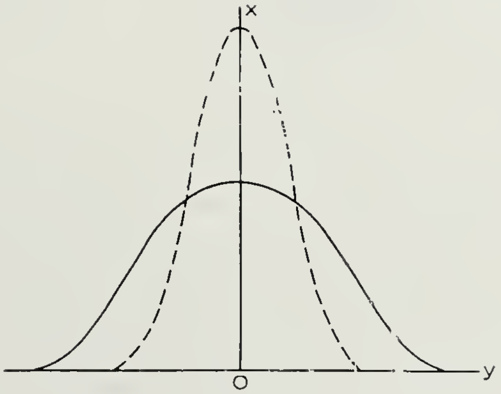

Fig. 24.
Cross-wind concentration downwind of a single source. - - -, instantaneous samples; ——, time-mean samples.

The shape of the concentration curve (see Fig. 24) indicates the width of the cloud of effluent. We may, if we wish, define the width in terms of the standard deviation of the Gaussian curve, as explained in books on statistics, or we may adopt the usual convention of defining the width as the distance from the axis where the concentration is one-tenth of the peak value. By means of this convention it is possible to discuss the major part of the cloud in finite terms while avoiding the infinite values of the width that apparently result from the employment of a Gaussian curve to describe the distribution of concentration.

Ground level source of pollution

In considering the effects of meteorological factors it is convenient first of all to take the case of a source of pollution at ground level. A cloud of smoke or other airborne substance generated continuously at ground level drifts downwind as a long plume, its width and height increasing with distance travelled in accordance with the degree of turbulence present. In the downwind direction from the source, *i.e.* on the axis of the cloud, measuring instruments would show that the concentration of pollutant is very high near to the source and decreases with distance.

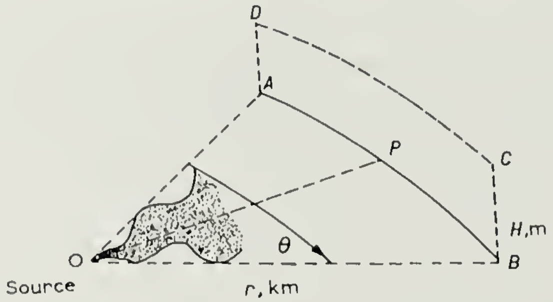

Fig. 25.
The boundaries of a cloud at distance r from a ground level source.

Fig. 25 shows diagrammatically the plume of pollutant extending downwind from a ground level source. As the plume passes over an arc of radius r centred on the source at O, let it be confined within an angle Θ subtended at O and a height H in the vertical. Following the convention for defining the width of the cloud, the concentrations at A and B are one-tenth that at P, and the concentrations at D and C are equal and of value one-tenth that at A or B. The physical dimensions of the cloud, as given by H and Θ, are determined by the meteorological conditions and when we know these values, or more commonly, estimate them, concentrations of pollutant can be calculated.

If we denote by X_g the concentration at the point P on the axis of the cloud (see Fig. 25) then its value is given by the following equation:

$$X_g = \frac{2.8 \cdot 10^{-3} \cdot Q}{u \cdot H \cdot r \cdot \Theta} \text{ units/cm}^3$$

in which Q = strength of source in units/min. *e.g.* pounds or kg released per minute, u = wind speed in m/sec, H = height in m, r = radius in km, Θ = angle in degrees (not in radians).

Of the various parameters in the above equation, Q and r will be known, u is obtained from anemometers or from weather charts, H and Θ must be estimated from a consideration of all the existing meteorological conditions. Before discussing separately how the vertical spread H and the lateral spread Θ may be expected to vary, it will be useful to present a broad classification of different weather situations designed to simplify the process of estimating the values of these two parameters. The categories of weather defined in Table 21 below are based on the preceding section, where the effects of wind and temperature gradient upon turbulence were discussed. From the above equation it will be seen that the concentration varies inversely as the wind speed: the greater the speed, the smaller the concentration.

TABLE 21

WEATHER CLASSIFICATION FOR ESTIMATING SPREAD OF A PLUME

Category	*Associated weather conditions*
(1) Lapse or unstable	daytime, sunny, wind 0–4 m/sec
(2) Slight lapse or slightly unstable	(a) daytime, sunny, wind 4 m/sec or more
	(b) daytime, cloudy, wind 0–4 m/sec
(3) Neutral	(a) daytime, cloudy, wind 4 m/sec or more
	(b) day or night, heavily overcast, all wind speeds
	(c) night, fairly clear, wind 4 m/sec or more
(4) Inversion or stable	night, fairly clear, wind 1–4 m/sec

The categories of Table 21 are by no means exhaustive; indeed the atmosphere seems to have an almost infinite variety of characteristics. Nevertheless a list such as that given in the table may be regarded as useful for summarizing an aggregate of weather conditions as a first step towards estimating H and Θ. Since the table gives little more than a crude classification, the estimates resulting should be interpreted as fairly realistic but with no claims to a high order of accuracy.

Estimation of vertical spread H

As the distance from the source increases the cloud or plume extends higher into the atmosphere. The rate at which this vertical spreading takes place depends mainly on the degree of stability in the atmosphere, *i.e.* on the vertical gradient of temperature. The slowest rate of spreading occurs when the atmosphere has great stability, as in the case of a pronounced inversion; the most rapid spreading is found in very unstable conditions. In Table 22 rough estimates of the increase of H with distance from a ground level source over the range 0.1–100 km are given for the meteorological categories already defined. These estimates of H, together with those of Θ below, are based on diffusion experiments carried out by Pasquill and members of his research group at Porton in England [357, 359].

In applying this table to any particular occasion, it is important to consider a deep layer of the atmosphere in case any discontinuities of temperature gradient are present. Quite frequently it may be found that while the atmospheric layer adjacent to the earth's surface is unstable with strong convection and mechanical turbulence taking place, the next layer above is an inversion and this would act as a barrier to further vertical spreading of the plume. This possibility—there are many others—illustrates the need for a close meteorological examination every time estimates of concentration are required or measurements have to be explained. In the example mentioned, vertical spread would be halted at the base of the overlying inversion. In the subsequent travel of the plume the Gaussian distribution of concentration in the vertical would be gradually transformed into a uniform one throughout the layer.

An important case is that of very light winds (less than 1 m/sec) on a clear night, *i.e.* conditions productive of sharp ground frost or heavy dew. In such circumstances the vertical spread is even less than that given in row 4 of Table 22. It is not practicable to give estimates for this example because the plume does not normally have any well defined system of travel.

TABLE 22

ESTIMATES OF VERTICAL SPREAD H AND LATERAL SPREAD Θ FOR VARIOUS METEOROLOGICAL CATEGORIES

Weather category	*Distance from source, km*							
	0.1	*1.0*	*10*	*100*	*0.1*	*1.0*	*10*	*100*
	H, m				*Θ, degrees*			
(1) Unstable	25	300	very large	very large	45	38	31	22
(2) Slightly unstable	20	150	1000	very large	30	25	20	15
(3) Neutral	10	70	300	1000	20	17	14	10
(4) Stable	5	30	100	200	10	9	7	5

Estimation of lateral spread Θ

For estimations of Θ it is best to have an anemometer, giving a continuous record of wind speed and direction, installed near to the source in a suitable exposure. Values of Θ can then be inferred from the fluctuations of the direction trace. The value of Θ for $r = 0.1$ km may be taken as the maximum width in degrees of the direction trace (see Fig. 25, p. 134) and half that value may be used for $r = 100$ km. The value of Θ to be used becomes smaller as the distance from the source increases because the form of the plume is not conical but more like a cigar.

Table 22 also gives specimen values of Θ for use in the weather situations described in Table 21.

It might here be mentioned that the Tables 21 and 22 have been drawn up not only on the basis of experimental results but also in keeping with the physical principles discussed in Section 4. The tables may indeed be regarded as illustrating the practical application of those principles.

Calculation of axial concentration

The ground level concentration on the axis of the cloud may now be calculated from the equation on p. 134 by substituting r in km, the estimated values of H in m and Θ in degrees, the appropriate value of u (the wind speed) in m/sec and the known strength, Q, of the source. The values of H and Θ for distances other than those given in Table 22 are obtained by interpolation.

The values of concentration so obtained are reasonably valid for fairly open country. However, if release takes place in a built-up area, additional turbulence and channelling of the airflow leads to increased values of H and Θ near to the source but not for greater distances. A practical adjustment to allow for a built-up area is therefore made by doubling the values of H and Θ given in Table 22 for the distance $r = 0.1$ km.

Concentrations from an elevated source

When the source instead of being at ground level is at a height h in the atmosphere, the main additional factor to be taken account of is that the plume now diffuses below as well as above the horizontal plane through the source and is reflected when, some distance downwind, it reaches a vertical depth h below the chimney mouth. An excellent description of the behaviour of effluent plumes is given in a publication of the U.S. Atomic Energy Commission[353]. In unstable atmospheric conditions, *i.e.* when the temperature decreases with height in the atmosphere, "looping" occurs; the width of the plume increases downwind, but the concentration at the ground is mainly controlled by large-scale eddies with periods of the order of minutes, giving the plume a wavy appearance. Diffusion is generally rapid but occasional puffs of high concentration may be brought to the ground very close to the source. When the temperature is nearly constant with height (neutral conditions), the axis of the plume becomes more nearly horizontal and the diffusion process is much steadier. Under inversion conditions, *i.e.* temperature increasing with height, vertical turbulence is strongly damped, and the vertical spread of the plume is much reduced; however, the rate at which lateral spreading proceeds may not be greatly affected. Diffusion of the plume to ground level may then be insignificant within several kilometres of the stack. It is possible, if there is a discontinuity of temperature gradient near the top of the stack, for diffusion to proceed more rapidly from the top than from the bottom of the plume or *vice versa*. Particularly important is the case of an inversion above the stack, with unstable conditions below. Rapid mixing in a restricted layer of the atmosphere then results and high ground concentrations are produced ("fumigation"). Such conditions are usually short-lived, occurring shortly after sunrise as solar heating breaks down a nocturnal inversion, but may occasionally persist for longer periods, *e.g.* in radiation fog.

The gases discharged from a stack generally emerge with an appreciable upward velocity and usually with a temperature above that of the surrounding air. Both factors help the plume to ascend well above the stack level, buoyancy being the more effective although a certain minimum velocity of efflux is essential if the plume is to avoid downwash caused by the eddies due to the stack itself. The theoretical prediction of the behaviour of effluent plumes is extremely complex and at present there seems to be no treatment of the problem that gives satisfactory results in all conditions. Papers of interest in this field have been contributed by Davidson[355], Holland[358], Priestley[362], Bosanquet[354] and Schmidt[363].

In terms of ground level concentrations, the effect of raising the source above the ground is that in the immediate vicinity of the chimney there is no trace of the plume, provided down draughts are avoided; beyond that the concentration begins to increase and rises to a maximum at a certain distance from the chimney. At greater distances the concentration at ground level falls off until eventually it approximates closely to that from a source at the ground. In other words, the principal effect of raising the source is felt at fairly short distances; at very large distances the benefit of raising the source is lost. The differences between an elevated source and one at the ground are illustrated in Fig. 26, which shows the variation of ground level concentration with distance along the axis of a plume for a release at the ground and for a release at a height of 100 m.

In general, for an elevated source at a height h in the atmosphere (h = height of chimney plus ascent due to momentum and buoyancy), the concentration along the axis of the plume is given by

$$X_h = \frac{2.8 \cdot 10^{-3} \cdot Q}{u \cdot H \cdot r \cdot \Theta} \exp \left\{ -2.3 \left(\frac{h}{H}\right)^2 \right\} = X_g \exp \left\{ -2.3 \left(\frac{h}{H}\right)^2 \right\}$$

where X_h denotes the concentration from a source at height h.

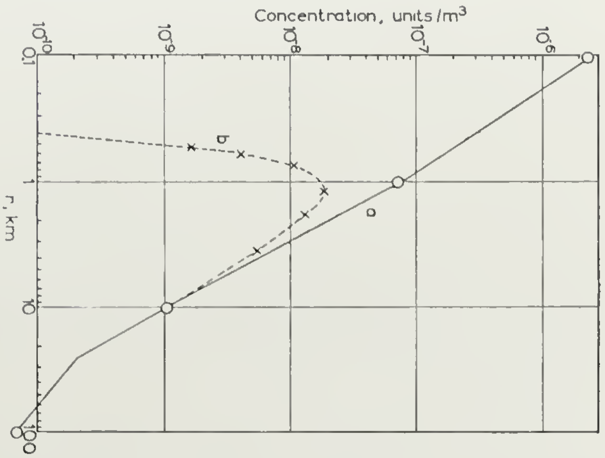

Fig. 26.
Variation of axial concentration with distance for source strength 1 unit/min. ——, release at ground level; - - -, release at a height of 100 m.

By comparison with the equation on p. 134 we see that X_h can be obtained directly from the corresponding ground level concentration by multiplying by the exponential factor given in the above equation. This factor depends on h, the height of the source, and on H, the vertical spread at the distance under consideration and estimated from Table 22. The following Table 23 gives some specimen values of this factor for various ratios H/h.

TABLE 23

VALUE OF FACTOR EXP $\left\{-2.3\left(\frac{h}{H}\right)^2\right\}$

H/h	0.75	1.0	1.5	2.0	3.0	5.0	10.0
Factor	0.02	0.10	0.36	0.56	0.77	0.91	0.98

From this table it will be evident that, unless the spreading H is greater than three-quarters of h, the height of the source, the ground level concentrations will be negligible. At distances such that H is greater than about $3h$, the elevation of the source ceases to be of much importance.

Estimation of maximum concentrations

For many problems connected with air pollution from chimneys, estimates of the maximum concentration likely to be experienced at ground level are of primary interest. They also form a useful first step if it is desired to use the methods already described to draw isopleths or boundaries within which concentrations may be expected to exceed specified values.

Sutton's theory[364] gives the following equations for the distance from a chimney at which the maximum concentration occurs and the value of that maximum:

$$d_{\max} = \left(\frac{h}{C}\right)^{8/7}$$

$$X_{\max} = \frac{2Q}{e \cdot \pi \cdot u \cdot h^2} \text{ (approximately)}$$

where C is a diffusion constant, and e and π have their usual meanings. The value of C varies according to the type of terrain over which the plume is travelling and may be taken as 0.12 over level grassland and about 0.25 over rough, hilly country.

The above equation applies to neutral atmospheric conditions and no formulae are available to give maximum concentrations in stable or unstable conditions. However, it is possible to give a broad indication of the main differences from the above equation when the vertical gradient of temperature is not zero. In lapse conditions, compared with a neutral atmosphere, the maximum concentration will occur nearer the chimney and be smaller in amount. In inversion conditions, the maximum will be higher than for neutral conditions and will occur further from the chimney.

Concentrations at points not on the plume axis

Knowing the peak concentration which is found on the axis of the plume and given by the equations on p. 134 or p. 138 depending on whether the source is at the ground or elevated, concentrations at points perpendicular to the axis at ground level are readily calculated from tables of exponentials. This is possible because the expression $\frac{r \cdot \Theta}{2}$ gives the distance from the axis at which the concentration falls to one-tenth of the peak value. Off-axis concentrations are therefore merely a matter of computing or reading-off the appropriate Gaussian curve.

Order of accuracy of estimates

It has already been remarked that estimates of concentration, however carefully made, are subject to numerous uncertainties. This word of caution is worth repeating because it is impossible to provide any basis of calculation that is applicable or can be adapted to all possible weather conditions. The calculations that are made on the principles outlined above are therefore only approximate estimates which give a good idea of orders of magnitude but should not be expected to have a high order of absolute accuracy.

The interpretation of concentration measurements

In recent years the number of towns and other communities which have organized measurements of atmospheric pollution has been growing rapidly. It is right that national and local authorities should be alive to the evils of pollution, which can only be demonstrated conclusively by routine observations, but there is also an obligation upon scientists, doctors and engineers to ensure that the measurements are logically studied and not merely left to accumulate. Observations of the distribution of pollution in a region can be summarized on their own account to give hourly, daily and monthly averages.

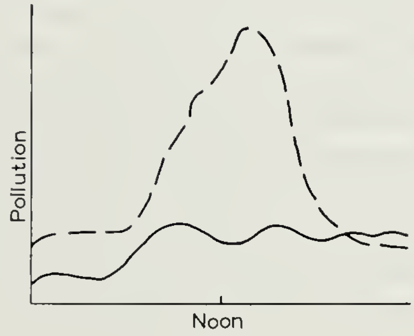

Fig. 27.
Diurnal variation of pollution at Leicester. - - -, in winter; —, in summer.

As an example, Fig. 27 shows the average diurnal variation of pollution in winter and summer at Leicester, a fairly large residential and industrial town in England. The differences in the two curves reflect the fact that much larger quantities of domestic fuel are used in winter than in summer and also the fact that turbulence is at a maximum in the summer months. The main causes of the variations from hour to hour in the shape of the two curves have been summarized by Meetham[361] as follows:

(1) the daily cycle in the rate of fuel consumption,

(2) the extra smoke emitted when fires are being lit in cold grates in the morning,

(3) the daily cycle in atmospheric turbulence.

Although summaries of pollution measurements alone are valuable in indicating diurnal and seasonal cycles, it is clearly not sufficient to treat these observations in isolation. They should of course be analysed in conjunction with health and other parameters—in fact, in many countries there is already a vast amount of data awaiting detailed study. The patterns of pollution in an area are most usefully examined together with simultaneous values of meteorological variables. Such studies provide a useful check on estimates previously made and also make important contributions to knowledge which may be applied in other localities.

Many detailed surveys of the distribution of pollution in an area have been made in various countries, especially in U.S.A. and Britain. In the latter country the Department of Scientific and Industrial Research made an intensive survey of the pollution in and around a particular town. The report, *Atmospheric Pollution in Leicester*[356], has provided much useful information of wide application. A more detailed study, this time of the pollution from a major, isolated source in a country district, was carried out by Meade and Pasquill[360], who applied diffusion theory to long period averages of pollution and obtained noteworthy results of statistical significance.

In stressing the need for detailed research on pollution observations, we also emphasise that such work should be on the widest possible basis involving as many as possible of the diverse interests that have at times too specialised commitments in the pollution field. In this important subject there is probably a greater number of separate disciplines concerned than in any other subject of social importance. Moreover the interests of one discipline are continually overlapping others, thus bringing to the forefront the need for collaboration in research.

Section 6. Smog - its Origin and Prevention[365-373]

by

P. J. MEADE

For most of the time the number of people who are mindful of air pollution as an evil is comparatively small. Sufferers from bronchitis and similar maladies, members of the medical profession and those immediately concerned with the implementation of public health acts have the subject of air pollution constantly in mind, on some days relieved at its apparent harmlessness and occasionally appalled at its severity. As a rule, however, the ordinary member of the public rarely stops to think about pollution in terms of the damage it causes—to health, to vegetation, to the paintwork on houses and to the stone and metal work of buildings—or in terms of its economic cost which in Great Britain has been estimated to be about £5 sterling per annum per head of population[372]. It takes a smog, indeed a bad one, to bring home to everybody that atmospheric pollution is a scourge which should no longer be tolerated in a civilized community.

Smog is the term used to denote the presence in the atmosphere of a mixture of smoke and fog. Although the term only came into use early in the present century and became widely adopted only a few years ago, smogs as such have occurred from time to time in industrial areas for several centuries, in fact, since coal began to be used extensively for the production of heat and power. In the thirteenth century the Parliament in England passed a law forbidding the burning of coal in London but eventually, as wood became scarcer and as its unsuitability as a fuel for the iron industry came to be realized, this law, which was worthily conceived, had to be abandoned. At first when the consumption of coal was on a modest scale compared with the energy requirements of today, the practice of discharging to the atmosphere the waste products of combustion was not of great consequence except perhaps in a few small localities. However, as fuel requirements both for domestic and for industrial purposes increased, this practice, which in the beginning was merely undesirable became almost imperceptibly a major threat to living organisms—human beings, animals and plants. For many years the magnitude and potential of this threat were recognized only by small bodies of dedicated people, such as the members of the Smoke Abatement Society (now called the National Society for Clean Air) in Great Britain who campaigned ceaselessly against wanton and uncontrolled pollution of the atmosphere. Thus although smogs, called by other names such as 'pea-soupers' and 'London particulars', were well known winter phenomena in large industrial areas, the public conscience was not widely aroused until the occurrence of large scale fatalities which could be directly attributed to smog. This is not to say that nothing was done anywhere. Indeed, in many industrial countries, such as the U.S.A. and Canada as in the West and in Great Britain and Western Europe, successive legislation over the past hundred years or more has sought to protect communities from smoke and chemical pollution. It must be recognized, however, that much of this legislation was introduced in spite of public apathy and only after strenuous efforts by a comparatively few far-sighted individuals.

It is probable that many smogs in the past have exacted a heavy toll in human and material casualties without the relationship between cause and effect being established. On such occasions it seems possible that the weather and not the pollution received the greater share of the blame. In the present century, however, three smog disasters have produced a sharp awakening in the public mind to the dangers inherent in fouling the air we breathe. In December 1930 in the Meuse Valley near Liége in Belgium a fog laden with gaseous and particulate impurities persisted for five days and caused the deaths of sixty-three people and serious illness to many more. The pollution came from such industries as iron and steel, potteries, zinc, glass, lime kilns, power stations and chemical works. The weather conditions which brought the fog and the configuration of the valley caused the air to lie stagnant throughout the five-day period. The point to note specially is the occurrence of conditions favourable for persistent fog and the presence of pollution sources.

The second disaster took place at Donora near Pittsburgh, in U.S.A. in November 1948 and resulted in nineteen deaths. In this case the primary source of polluton was a zinc smelting works discharging sulphur dioxide to the atmosphere. As in the earlier incident in Belgium, the topography at Donora was that of a steep sided valley which combined with the foggy situation, again over a five day period, to prevent the dissipation of polluted air. Another coincidence between Liége and Donora was that the mortality, expressed as a percentage of exposed population, was of the same order of magnitude in each case.

The notorious London smog of December, 1952 provides the third example. This smog, which lasted four or five days, caused at least 4,000 deaths and much illness, and therefore must be regarded as the most disastrous event of its kind that is known to have occurred anywhere in the world. Detailed studies of the London smog have been practicable because of the adequate amount of relevant data covering weather conditions, pollution measurements and medical histories that became available. Moreover, as a result of public and official anxietyaroused by this smog, the Government of the United Kingdom set up a Committee, the Beaver Committee [366, 367], to examine the nature, causes and effects of air pollution and to make recommendations as to preventive measures.

A notable feature of the London smog was that topography, which played so important a part in the Liége and Donora incidents, was not a contributory factor. The stagnant and heavily polluted fog in London existed as a more or less central core within a large area of fog which was only moderately polluted near its outer edges. The meteorological aspects of the smog have been discussed by Douglas and Stewart[368]. On 5th December, 1952, almost the whole of England was covered by the central region of an anticyclone and it was not until four days later that these quiet, calm conditions moved away in advance of freshening winds from the South-West. During the whole period from 5th to 9th December the barometric pressure was remarkably uniform over London and neighbouring areas. Conditions were therefore ideal for the development and persistence of fog. Another factor to which medical authorities have attached significance was the unusual coldness of the fog. In the areas principally affected air temperatures near the ground hardly rose above the freezing point, whereas at places just beyond the fog belt temperatures approaching 40° F were recorded. The lowest temperatures experienced were around 23° F.

The pollution aspects of this smog have been examined by Wilkins[373], using observations of smoke and sulphur dioxide concentrations made over an extensive network of stations. He also compared the pollution trend with the mortality, using data published by Logan[370]; Fig. 28, taken from Wilkins' paper, shows in one diagram the daily levels of air pollution and of deaths in the fog area. This figure, which is factual is perhaps the most devastating indictment of air pollution that can be presented.

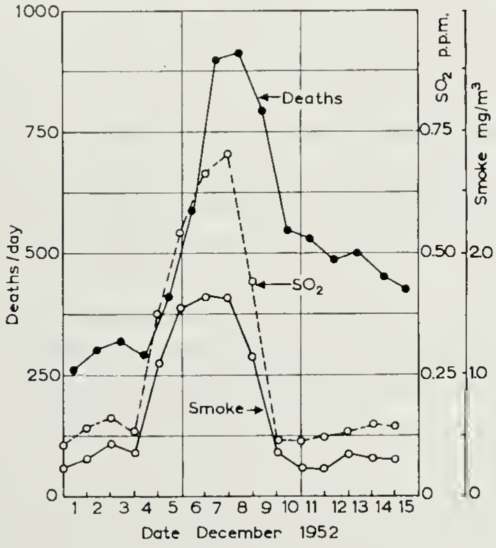

Fig. 28.
London smog, December 5th-9th, 1952. Daily air pollution and deaths.

An interesting and in many ways comprehensive analysis of this remarkable smog has been given by Meetham[371], who considered, *inter alia*, the heat and water balance of the fog and the life cycles in suspension of the various impurities—smoke, sulphur gases, halogens and oxides of carbons. He estimated rather roughly that in equilibrium the fog, covering an area of 450 square miles, contained 380 tons of smoke and 800 tons of sulphuric acid.

We have discussed the London smog at some length but not to the extent that reference to the papers mentioned above is no longer necessary. This particular smog serves as an invaluable example because it is probably the best-documented case of its kind and also because the lessons it provides appear to be fairly conclusive. Smogs have, of course, occurred in England since 1952, fortunately with less severe consequences, but for the most part they confirm the inferences previously drawn. There are also the somewhat unique smogs of Los Angeles, the harmful effects of which appear to have their orgins in ozone and in chemicals produced by the action of ozone on hydrocarbons which are released to the air by the burning of petroleum in automobiles and by industry[365]. Whereas the smogs of Great Britain and those of Los Angeles are fundamentally different, the former occurring in a reducing atmosphere and the latter in an oxidizing atmosphere, the associated weather conditions have much in common—stagnant air and inversion conditions giving a liability to fog formation.

The weather conditions are from many points of view the key to the smog problem. On most occasions the atmosphere is reasonably efficient in its power to transport and disperse pollutants so that, at distances not far removed from their sources, concentrations are virtually negligible. However, when an inversion layer exists, the air in that layer is relatively inefficient as a dispersing agent, because turbulence is damped down, and not very effective as a transporter of pollutants because inversions tend to reduce wind speeds. If, therefore, an inversion occurs in an area where considerable amounts of impurities are discharged to the air, the danger of a smog must arise. Moreover, if the inversion persists for many hours or even several days, there must then be a high probability that the resulting smog will increase the death and sickness rate in that area as well as causing other serious damage.

It so happens that not all smogs have the appalling consequences of those which occurred at Liége, Donora and London. These cases are widely quoted as examples but by concentrating on them we may perhaps obscure the cardinal facts that smogs are of quite frequent occurrence and that all smogs are harmful. In Britain the winter of 1958–59 was noteworthy for a large number of smogs which at different times affected many industrial areas. In Glasgow alone it was estimated that damage amounting to £50,000,000 was done by an abnormal incidence of smog. Meade has examined the meteorological aspects of these smogs and has stressed their association with a particular set of weather conditions.

The main lesson to be drawn is that the worst smogs occur in conditions of persistent fog and the latter are found in quiet anticyclonic conditions. Now, in summer anticyclones give generally fine weather, ideal for holidays, but in winter the situation may be very different. Then the central region of an anticyclone with its light or near calm winds may produce a stagnant situation with a persistent inversion which prevents the escape of pollutants. If the anticyclone becomes stationary, the smog conditions must progressively become worse unless, of course, the emission of pollutants were stopped at the onset of the fog. The winter is the important season, except in the case of Los Angeles smogs, because at that time the incoming energy from the sun may not be strong enough to penetrate and disperse a fog once it has formed and relief may not come until the anticyclone moves away from the affected area.

The two fundamental factors in severe smogs are, therefore, the pollution and the anticyclone that has become stationary. The one factor is man made and must be regarded as controllable, given the will; the other factor, the weather, is not subject to control and, one may forecast, never will be. While the average tracks of anticyclones are well known to meteorologists, the history of an individual high pressure system is liable to small but important departures from the average. The annual variations in the positions of anticyclones can largely account for the differences in the location of smogs from one year to the next, that is, may explain why London is the worst affected one year and Glasgow or Manchester another. And these annual variations cannot be predicted in detail for any appreciable time ahead.

Not only is it impossible to control the positions of anticyclones as a means of avoiding smog; it is also out of the question to disperse smog, or even fog, by artificial means. Admittedly it is practicable by burning huge quantities of fuel oil to clear fog sufficiently from a limited area of runway in order to permit the landing of aircraft, but the cost of such measures is enormous and, if one were living on the runway, the fog would be infinitely more tolerable than the remedy. The idea of fog clearance has always been an attractive one and to many, who contemplate the achievements of modern technology, not impossible of achievement. In ruling out this proposal as a cure of the smog problem, therefore, we should also point out that it would be even more difficult to clear smog than fog. It is common to almost everybody's experience that the clean water fog of a rural area disperses earlier and more rapidly than the polluted fog in a neighbouring industrial or residential area. This is because the airborne pollutants, some of which are attached to water droplets while others are in suspension, are effective in making a fog denser and more persistent.

Since the main weather factors, the anticyclone and the fog, cannot be subordinated to human control, it must be conceded that the only means of preventing smog lies in the wholesale reduction of atmospheric pollution. This conclusion is in agreement with the findings of the Beaver Committee, already referred to above, which recommended the establishment of large smokeless zones, in which the emission of smoke from chimneys would be entirely prohibited and the replacement of bituminous coal by smokeless fuels for domestic purposes. Such measures strike at the root of the smog problem but, for their complete fulfilment, attention must be given to the individual sources of pollution—industry, power stations, road traffic, collieries, domestic users and so on. Of these sources domestic chimneys are probably the greatest offenders. However, smog is essentially a fairly local problem and, although it is appropriate to consider the relative guilt, it is necessary to pay attention to all sources if success in smog prevention is to be ensured.

Measures to reduce pollution, whether backed by legislation or merely depending on the voluntary co-operation of the people, must inevitably take a long time to become fully effective. The evil is long established and cannot be abolished in a day. A worthwhile procedure during the transition period consists in the application of a form of meteorological control which would come into effect whenever the weather conditions in a particular locality became favourable for the formation of fog and, therefore, of smog. This does not mean that at such times meteorologists would assume control of local industries but rather that managements, on receipt of a warning forecast, would themselves take steps to reduce substantially the amount of pollution discharged to the atmosphere. Action on these lines has been tried successfully in U.S.A. and in Canada. Hewson[369], for example, has described how emissions from a smelting plant in Trail, British Columbia, are varied in accordance with meteorological conditions. Before this system was instituted, much damage was done to vegetation in the neighbouring State of Washington and a great deal of international litigation resulted. As Hewson has stated, the principles could be applied in almost any locality.

To sum up this discussion, we emphasize that the specific remedy for the smog problem lies in the abolition of air pollution. Disasters such as Liége, Donora and London are merely peaks in an ever present situation and it would be wrong to ignore the main problem while taking small measures as the sequel to each disaster. There is no doubt that it is the will of the public that smog must end. The public may also have to assert its will to ensure that the means are taken to achieve the end.

CHAPTER 5

Possible Influence of Extra-terrestrial Factors (Piccardi Effect)

In all periods of human civilization, right up to the present day, many people have believed in the great influence of extra-terrestrial phenomena on the living organisms on earth. Much has been written on this subject; only some of the more scientific publications have been cited in the list of references[374-446]. One of the best critical summaries was that prepared by Berg[376], Professor of Meteorology at the University of Cologne. Students interested in this problem are strongly advised to read Berg's review; also Stetson's publication[435]. Stetson was formerly Director of the Cosmic Terrestrial Research Laboratory at Needham, Mass. (U.S.A.).

In most of the published scientific papers the study of the possible influence of the cosmic space outside the earth is confined to the influence of the sun. It is generally realized that, without solar heat, life on earth would be impossible. On pp. 22, 88 and 90 we also mentioned the significance of solar radiation on the ozone production of the atmosphere and the importance of this gas to the weather conditions on earth and to biological life in general.

Another well-established fact is the influence of solar eruptions on *magnetic storms* and the *northern lights* on earth. A few general remarks may help to clarify these effects.

The brilliant round disc of the sun which emits light and heat is known as the *photosphere*. Overlying this surface is a shell chiefly composed of hydrogen gas and calcium vapour, known as *chromosphere*, which is only clearly visible as a red shell during total eclipses of the sun. It is divided into a lower part of a few hundred miles, the *reversing layer*, composed of many of the familiar terrestrial elements, and the true chromosphere, composed mainly of hydrogen and helium, extending several thousand miles in space. It is from this chromosphere that huge bursts of hydrogen gas are observed, known as *prominences* or *protuberances*, which may attain in a few minutes heights of 100,000 miles or more in space.

The chromosphere is surrounded by an outer envelope of very great height and exceedingly small density, known as the *corona*. It is only observable during total eclipses of the sun.

On the surface of the photosphere darker spots occur, the *sunspots*, which seem to be areas of relatively lower temperature (about 1500° C) than that of the surrounding areas. According to G.E. Hale's observations with a spectroheliograph at the Mount Wilson Observatory in California in 1908, the sunspots are actually giant cyclones in the sun's atmosphere comparable with tropical hurricanes. While most ordinary sunspots are themselves big enough to contain the entire earth, the largest sunspot reported so far (7 Feb. 1946) was 90,000 miles in diameter. If one includes the associated spots, a total surface of 60,300,000,000 square miles was composed of sunspots *i.e.* 30 times the earth's surface. As this huge spot passed across the sun's disc, transatlantic radio communications were seriously disturbed and the northern lights were most spectacular.

Studies by Sanford in 1936 (ref.[431]) indicated the effect of planetary positions on sunspot frequency and radio reception. His observations were confirmed and amplified by J. H. Nelson[411] at the R.C.A. Communication Inc., New York. Both sunspot configuration and transatlantic radio disturbances seem to be closely related to the position of the earth and planets in relation to the sun.

Appleton and Stetson were able to demonstrate that, owing to the attraction of the moon, a tidal bulge in the ionosphere is created of rougly 1 km, seriously affecting radio reception (for further details see ref.[411]). During solar eclipses, disturbances of the electric *potential gradient* of the atmosphere (see p. 77) were also observed by J. T. Wilson and others. In other words, the sun seriously affects the electric field of the earth's atmosphere (see pp. 76) This is partly due to the visible radiations (light and heat) emitted by the sun, but it is more especially the result of various invisible radiations, which were classified by Siedentopf[434] as follows:

(1) *Short wave radiation*: wavelength 1 cm–20 m, created by electrons of the corona.

(2) *Ultraviolet and X-ray radiation* (known as *W-radiation*)*: various groups have been distinguished, *e.g.*, those with a wavelength of 2000–3000 Å, which derive from the photosphere and which are responsible for the dissociation of O_3 molecules in the atmosphere; 1300–2000 Å also from the photosphere causing dissociation of O_2 molescules on earth, etc.

(3) *Corpuscular radiation* (known as *P-radiation*): either with a velocity

* Recent studies during the Int. Geophysical Year have demonstrated the presence of intense X-ray radiation at altitudes of about 30,000 m, during solar flares. This intense radiation does not reach sea-level because of the absorbing effects of the atmosphere. It is probably caused by electron emission from the sun.

of 500 km/sec if formed in the corona (causing small magnetic storms), or 1600 km/sec if derived from the chromosphere; these eruptions cause heavy magnetic storms, northern lights, etc.

(4) *Ultra radiation*: with an energy of $5 \cdot 10^9$ eV, which derives from the chromosphere and affects the cosmic radiation.

In view of the data given above, there can be no doubt about the influence of the sun on important meteorological and physical factors in the atmosphere. So far, however, it has not been possible to find consistent and simple relationships between, say, the average temperature or precipitation in the atmosphere and solar activity.

In 1775 the Danish astronomer Horrebow discovered a *sunspot periodicity* of approximately 11 years, during which the number of sunspots increases or, decreases. This was later confirmed by Schwabe and Dessau in 1843 and by Wolf around 1880. The average interval is 11.13 years (according to Newcomb) but the intervals may fluctuate between 7.3 and 17.1 years. The rise to a maximum is usually more rapid than the fall.

Numerous studies have been published on the statistical relationship between these variations in sunspot activity and various biological phenomena (see list of references); but as very few of these studies can stand up to serious criticism, I should like to refer the interested reader to the publications of Berg[376] and Stetson[435].

So far, the only experiment which seems to show a consistent relationship with solar activity and which has been carried out since 1951 by a number of research workers, is that devised by G. Piccardi and described in a series of publications[413-424].

Piccardi, who is a Professor of Physical Chemistry at the University of Florence in Italy, worked out a simple inorganic, easily reproducible test, which has been carried out daily for many years in Florence. The same test has been succesfully repeated in several important scientific centres in Europe and during the last two years in Japan also, as well as in other parts of the world (Belgian Congo, Madagascar, Kerguelen Island, etc.).

In the experiment bismuth chloride ($BiCl_3$) is hydrolysed:

$$BiCl_3 + H_2O \rightarrow BiOCl + 2\,HCl$$

Bismuth oxychloride is insoluble and precipitates. In the experiment 35 g $Bi_2(CO_3)_2$ are dissolved in 1 l 1.5 N HCL. Twenty-five ml of distilled water are added to 5 ml of this acid solution. A whitish colloidal solution is formed and soon afterwards BiOCl precipitates. The mixing is carried out in a specially constructed mechanical mixer which excludes differences in personal handling of the experiment.

Two types of water tests are carried out: one with normal tap water, one with so-called "activated" water. The latter is prepared by putting a glass globe in the water. One drop of mercury and one of neon at reduced pressure are enclosed in this globe. Movements of the globe create an electric charge in the neongas. Experiments have shown that water touching the glass wall of such globes, has different physico-chemical properties.

The experiment is intended to show whether the precipitation with active water is quicker (T-experiment) or slower (R-experiment) than with ordinary tap water. After a series of 10 tests, the percentage of experiments which proved to be T-tests is noted. These experiments are carried out both in a metal-free chamber (F-test) and in a chamber where the test tubes are completely covered by a copper sheet of 1 mm thickness (D-test). It was found that the percentage values of T are different under the experimental conditions F and D.

The following results were obtained after a series of over 200,000 tests since 1951:

(1) In both F and D-tests the T-percentages on the whole decreased from 1951 until part of 1954, after which the values were rising.

(2) The T-percentages in the metal-free condition (F) show a yearly fluctuation with a maximum around February.

(3) The T-percentages in the metal cage (D) showed a low minimum around mid-March.

(4) Becker[375], of the Fraunhofer Institut at Freiburg (Germany), using 5-day averages of the precipitation values in the D-test, found a statistically highly significant correlation between the Piccardi's precipitation curves and the curve of the daily *relative sunspot numbers* (R)*. The F-tests seem to correlate better with solar eruptions and magnetic storms.

(5) High percentages for T were found in the metal-free chamber, during days of solar eruptions, whereas this relationship was lacking in the copper shielded cage.

(6) In a new series of tests the difference in precipitation was determined of normal water only but in the metal-free and copper shielded cage. The results of this P-test were recently confirmed by a group of Japanese physiologists (Itoh *et al.*[404]) of the Physiological Department of the Hokkaido University in Japan. It was found that if, instead of the bioclimatological reaction, the bloodclotting time of rabbit blood (using the method of

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* The relative sunspot number is a concept introduced by R. Wolf in 1848.

$$R = K\,(10\,g + f)$$

in which K = constant depending on the instrument used for observation, g is number of sunspot groups, f = number of single sunspots.

Sahli and Fonio) was determined both outside and inside the copper box simultaneously, the ratio of both clotting values was low when the "T" percentages were low and *vice versa*. In other words, when the rate of colloidal precipitation of bismuth is slower in the copper box than outside of it, the clotting time of blood is also slower in the box. A statistical analysis indicated that the results are highly significant. Similar observations were made previously by Giordano[401] in Italy. Experiments by Piccardi have shown that electromagnetic waves with wavelengths of a few kilometres also retard the precipitation speed in the P-test.

The significance of Piccardi's observations to biometeorology in general, if confirmed in future studies, is evident. There is no reason to assume that the organic colloids in the living organism would not be affected in the same way by this unknown extra-terrestrial radiation. However, in view of the extreme complexity of the problem and the lack of knowledge of the deeper physical mechanism involved in these tests, it seems premature to look for biometeorological applications at the present stage of research. The results obtained by Piccardi and his colleagues during the next few years will nevertheless have to be carefully watched, as, for one thing, they may give us a clue to the cause of yearly changes in the physico-chemical state of the blood of larger population groups. This will be discussed on p. 318.

PART III

Biometeorological Methods

Section 1. Causes of Slow Scientific Progress in Biometeorology

Whereas "long-periodical phenomena", due to seasonal weather or climatic changes of long periods are fairly well known in medical biometeorology, the daily influence of weather changes on the physiology and pathology of man is extremely difficult to demonstrate in a way which complies with modern scientific standards. Moreover, regional differences in climate between countries and between areas in the same country and their effect on the behaviour and pathology of man are easier to demonstrate than these daily weather influences. The main reasons are the following:

(1) A certain biological effect, as a result of specific weather conditions, does not show up in every person at the same time and in the same degree. This is due primarily to the fact that every person has a different genetic background; furthermore, their physiological "experiences", particularly during the days or hours preceding the weather action, are different. Modern physiological studies have clearly shown that preceding experiences may affect the outcome of a physiological experiment (see p. 199). But, apart from these reasons, another important factor is the difference in *morbidity limit, i.e.* the general level of the physiological equilibrium and general resistance of the body, which have to be passed before a given pathological process can be initiated. As this morbidity limit differs in different people at the same moment but also varies in the same person at different periods, we can never expect all in a large group of persons to respond to a given environmental stimulus—in this particular case the phenomenon of meteorotropism—at the same moment and in the same degree. We can only expect a *statistical correlation*; in other words, a given clinical phenomenon appears more often during certain weather conditions than can be expected on grounds of purely statistical probability.

(2) If we try to find some correlation between weather and clinical phenomena, we do not know beforehand whether the beginning, end or moment of maximal development should be correlated, moments which can be very far apart. Nor is it known whether a particular clinical phenomenon coincides exactly with the moment when some or other weather action begins, or whether it precedes or follows this moment by several hours, days or even weeks. Although several statistical methods have been devised to try out these various possibilities (see p. 176), some relationships are still not found owing to a more complex relationship between weather and clinical phenomena.

(3) General progress in biometeorology is also hampered by the following

four important points: (*i*) In the past, cooperation between meteorologists or geophysicists and medical practioners has been very poor. Representatives of each discipline are inclined to believe that they and they only are competent to study these problems. As a result, meteorologists without medical training have published incorrect clinical material and physicians have used untrustworthy meteorological data. It was not until recent years that a better team spirit began to develop in some research centres. (*ii*) Lack of sufficient statistical experience has often been responsible for publication of articles which should not have been published, because the reported correlations do not exceed chance probability. (*iii*) Many claims have been made, which were based on either very restricted or untrustworthy clinical material collected during short periods. Publication of the results with an impressive statistical analysis may give the erroneous impression of a highly scientific study. As a result, conclusions are copied by others, whereas in reality the basic material is insufficient and should have been enlarged. (*iv*) Often meteorological averages are used for the study of a certain clinical phenomenon. This is not correct, because, for example, temperatures fluctuating daily only 0.5° C around a monthly average have a biological effect entirely different from that caused by wide temperature fluctuations, although the averages in both cases may be the same.

We have deliberately stressed these various points because criticism, both justified and unjustified, has hampered the development of this relatively new medical science, new in the sense of the scientific methods which are applied in modern biometeorological research.

On p. 9 we briefly described the difference in scientific approach between *empirical* and *experimental* biometeorology. In the following pages we shall discuss these methods more fully.

Section 2. The Empirical Method

Two fundamentally different methods have been used in empirical biometeorology, the indirect or medical geographical method and the direct biometeorological method.

Indirect or medical geographical method

In countries where accurate mortality or morbidity figures are available and also the age structure of the population is known, it is possible to prepare *geographical distribution maps,* so called. The basis map is usually an ordinary administrative map giving the boundaries of the smallest administrative units in a country, either municipalities, counties, boroughs, or the like. The *standardized* mortality or morbidity figures are given in each of these units, *i.e.* the mortality or morbidity per 1000 (10,000 or 100,000) inhabitants of a special age group. For certain diseases the total of all age groups can be used; in other instances (for example cancer), when the incidence of the disease is predominantly developed in older or younger age groups, it is necessary to standardize on the population of that particular age group. Once the figures are indicated in each administrative unit of a geographical map of an area, certain mortality intervals are selected which are indicated by the same colour or black and white hatching, *i.e.* the mortality figures 0–25% above the country average are given the same colour, 26–50% another colour, etc. As a rule, a colour system from light to dark is selected with increasing mortality or morbidity. An example of such a geographical distribution chart is given in Figs. 29 and 30, which represent the geographical distribution of mortality from broncho-pneumonia in the Netherlands for the periods 1900–1930 and 1947–1953, the western part of the country being low, the eastern part having relatively high mortality figures.

The boundary, a S.W.-N.E. line, does not coincide with a line separating racial groups, areas with different food habits, medical facilities and so forth. Once such a map is prepared and it is demonstrable that differences in diagnostic accuracy, medical facilities, social or racial differences, etc. cannot account for the observed boundary (assuming that the medical death certificates are trustworthy, which is not the case in every country), we can compare these medical geographical maps with climatic maps and we may find, as in the case of this bronchitis map for example, that the boundary roughly coincides with a climatic boundary in the country. Similar studies could be made for other diseases.

Direct biometeorological method

This is the more common method and offers a readier means of discovering possible relationships between weather, climate and diseases.

Each biometeorological analysis of clinical data on an empirical basis requires two groups of observations, accurate *meteorological* data (compiled in specially devised biometeorological logs) and *clinical* data.

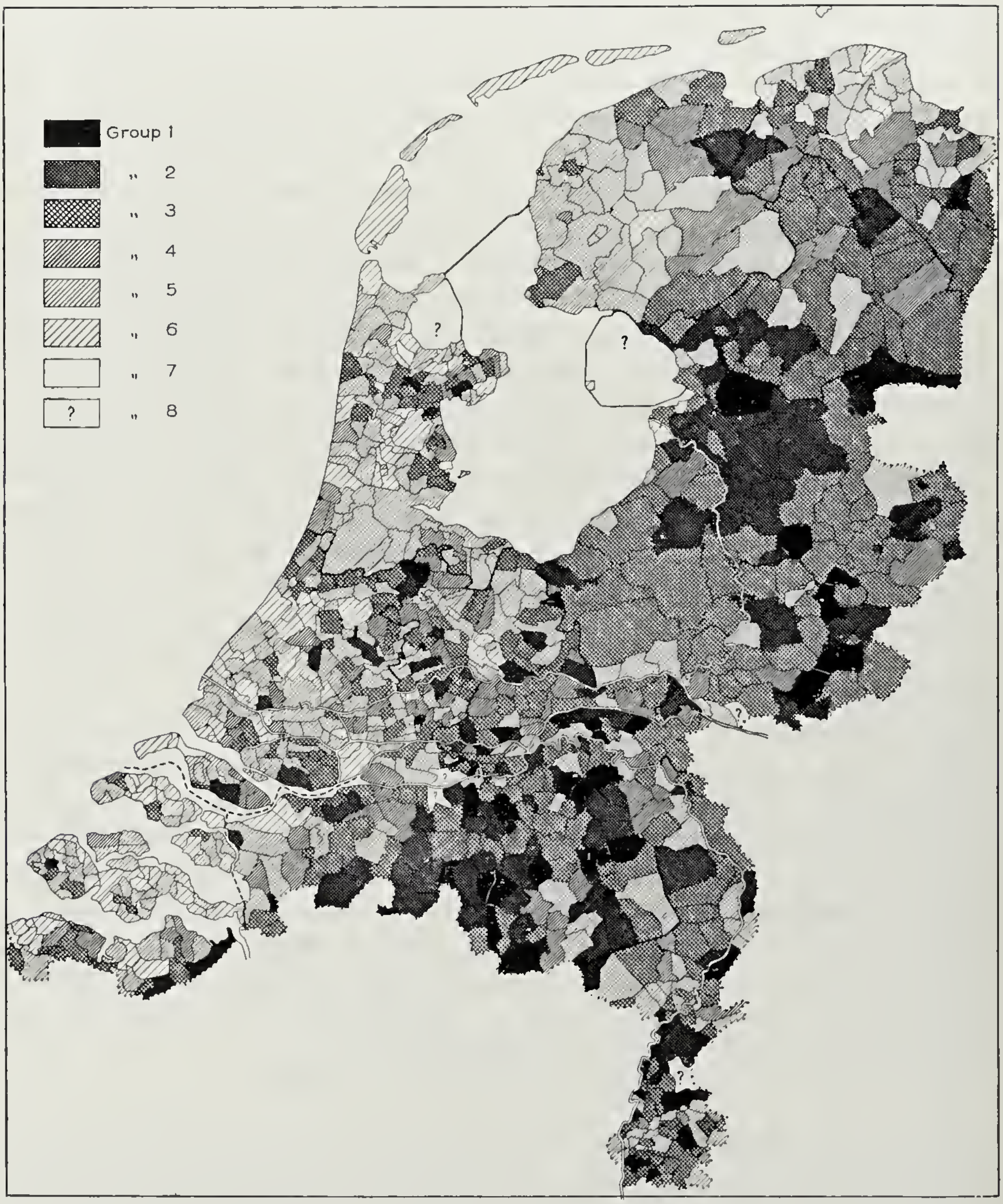

Fig. 29.
Average yearly death rate from all types of bronchitis and pneumonia as primary cause of death (period 1900-1930), based on data of the Netherlands Central Bureau of Statistics, compiled by J. C. Diehl and S. W. Tromp.

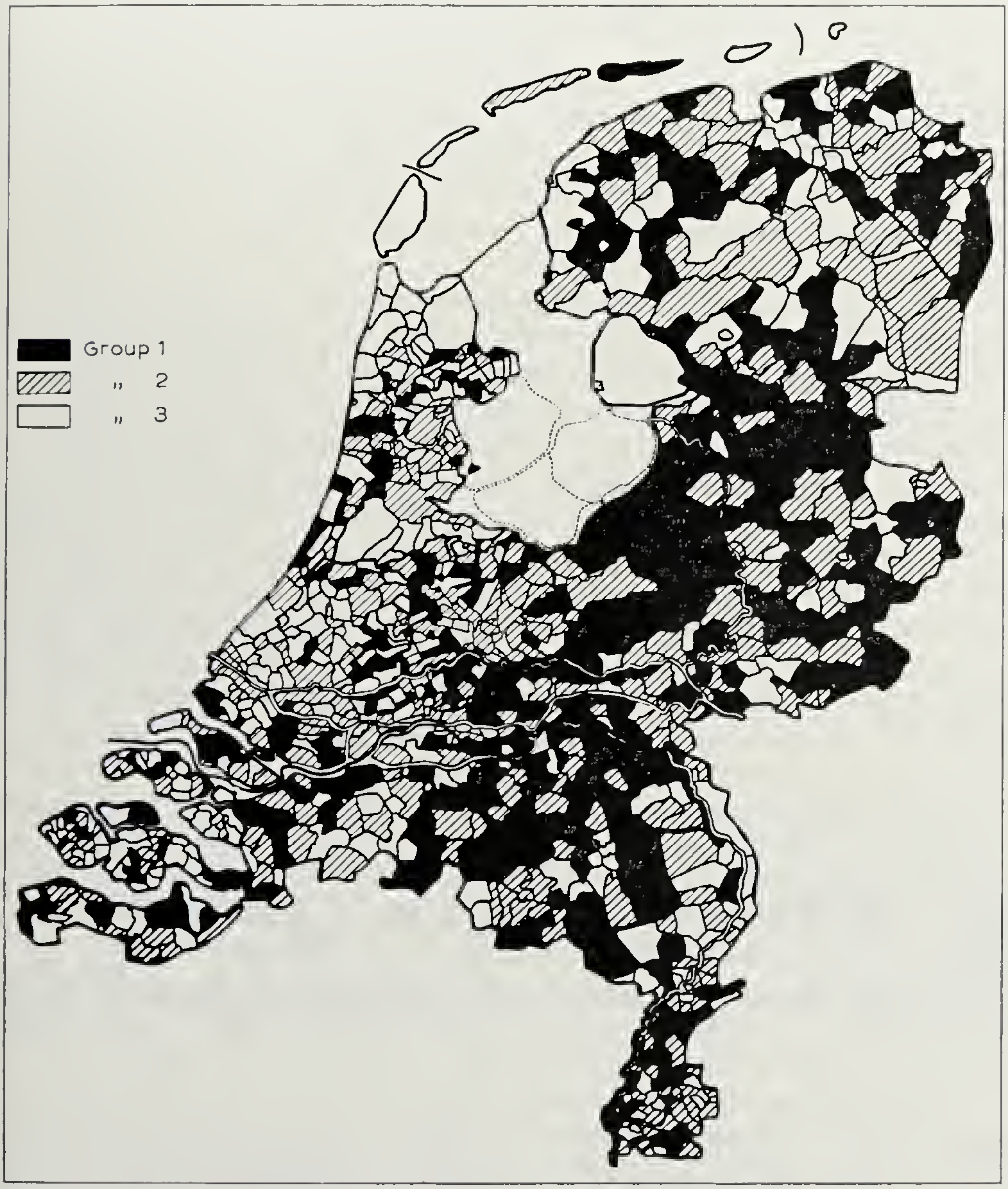

Fig. 30.
Average yearly death rate from all types of bronchitis and pneumonia as primary cause of death (period 1947-1953), based on data of the Netherlands Central Bureau of Statistics, compiled by J. C. Diehl and S. W. Tromp.

Subsect. A. PREPARATION OF BIOMETEOROLOGICAL LOGS

The various meteorological components described on pp. 33-81 should be recorded if possible in the centre of the area where the biometeorological studies are carried out. For some components, such as passages of weather fronts, air mass and electromagnetic impulses, the data can also be used for biometeorological analyses of clinical phenomena occurring in more distant areas.

In Fig. 31 an example is given of a *biometeorological log* as used by the Bioclimatological Research Centre at Leyden, the Netherlands. It will be evident that not all Research Centres will record the same meteorological components; also the symbols used will be different. The symbols should be adapted to the specific purposes of the biometeorological studies and they therefore usually differ from the international meteorological symbols. *E.g.,* in a very humid country like the Netherlands relative humidities below 50% are more important than high humidities and for this reason all values of less than 50% are marked in black in the log. The very high humidity values can be given the same colour in hot and arid countries. Since 1959 the biometeorological log of Fig. 31 has been improved by the addition of several important biological temperature indices (see also p. 41). As will be described on p. 330 a close relationship exists between the daily diuresis, 17-ketosteroid secretion, acidity and chlorine content of the urine and the general cooling in the atmosphere which is a function of temperature, humidity and wind speed. They are closely related to sudden influxes of polar or tropical air and the passage of fronts. Kata-thermometer recordings (or those of similar instruments indicating the actual cooling effect of the atmosphere) should also be included in the biometeorological log.

Such logs consisting of a combination of both physical and biological data could be used as a basic chart for the study of the possible relationship between certain clinical phenomena and specific weather conditions.

Whereas most of the data indicated in Fig. 31 can be recorded at a small local station, the data on air masses and fronts should be studied in relation to the regular *synoptic weather charts* (*i.e.* charts showing the weather conditions over a large area at a given instant of time) published by the official national meteorological institutes.

Subsect. B. METHODS FOR COLLECTING CLINICAL DATA

In biometeorological studies, either the clinical or physiological data of one patient or healthy person are followed daily for a considerable period

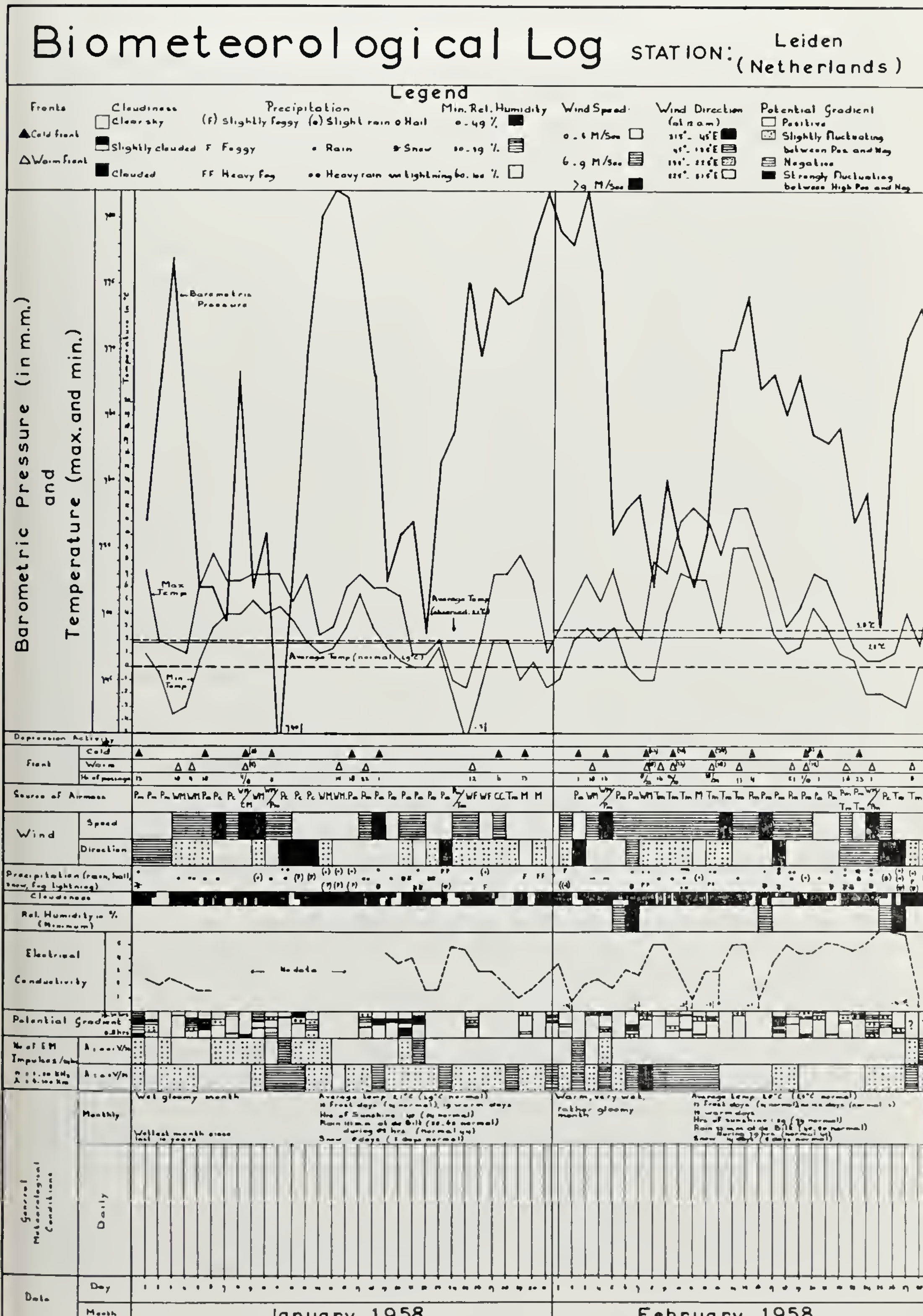

Fig. 31.
Example of a biometeorological log (January-February, 1958).

of time, or the data of a large group of persons are daily recorded. The advantage of using only one person is the fact that the problem of biological variation, which arises if more patients are studied, can be eliminated. On the other hand, the phenomena observed in one or only a few healthy persons or patients, particularly if they differ in age group, sex and profession, may not be representative at all for the population as a whole. Therefore, a large group of healthy people or patients (suffering from one particular disease), if selected at random will give us a better impression of the weather relationships in a larger population group than will a single patient. We may also discover a number of weather relationships which do not always show up in one and the same person. Once certain relationships have been established, it is advisable to study the individual cases separately in order to be able to carry out experiments as described on p. 168).

In Figs. 32 and 33, two examples are given of the forms used for patients at the Bioclimatological Research Centre at Leiden, *viz.*, for the study of the relationship between weather and climate and mental diseases and of that between weather and bronchial asthma. Besides severity of the complaint, other details are given, such as the medical treatment applied, possible causes of exacerbation and the like. Such forms are either filled in by the patient himself (which has proved to be very successful in the case of adult asthmatic patients), or by the sister or doctor in charge of a ward in a hospital or clinic.

The daily complaints of all the patients are transferred to larger tables. From these tables the daily percentage of patients (of a constant group of persons) suffering from a certain disease, but also the daily extent of their complaints, can be calculated. For this purpose the state of the complaint is given as an imaginary figure, 1, 2, etc. The percentage and severity figures are represented graphically in large clinical charts, the scale of one day being the same as in the biometeorological log.

Despite all the precautions taken, there are various reasons why the records should be accepted with all due reserve:

Errors in diagnosis. Although a point is made of using quite large groups of diagnoses (as otherwise differences in opinion between physicians may more easily arise), it should nevertheless be realized that a mental disease like schizophrenia—and even bronchial asthma, for example—are far from homogeneous diseases. Many varieties are known and there is no reason to assume that each variety would react in the same way to the same environmental factors (*e.g.* weather and climate).

Errors in recording. Psychiatrists and nurses, being fallible like all human beings, are liable to make errors in their daily recordings, partly on account of personal momentary inattention, distraction or preoccupation and partly on account of day-to-day differences in accuracy. The lack of homogeneity in the clinical material and the various methods of recording used by different physicians in the many clinics may well add to these errors. However, the use of data from different institutes has the following in its favour: (*i*) The total number of patients is considerably larger. It is evident that to record the detailed condition of a patient four times a day for a whole year imposes an enormous strain on the nursing staff. Seldom, therefore, can the same physician or sister-in-charge keep the records of more than ten patients at a time. (*ii*) Recording errors made by one sister or physician, or the possible effect of ill-temperedness on the part of the nursing staff on some particular day owing to psychosomatic or other factors, will hardly affect the percentages obtained for all the clinical data.

Errors due to medical treatment. As many patients are under constant medical treatment, their reactions to environmental factors are not natural. For instance, the reactions of mental patients will be weakened as the result of treatment with largactyl and other tranquillizing drugs. Therefore, high peaks of restlessness observed may represent only a minimum and not the maximum exacerbation of complaints created by environmental factors.

Possible errors due to "unpleasant" weather conditions. One might be inclined to assume that poor weather conditions (heavy rain, hail, storms, etc.) would immediately affect the restlessness and temper of the nursing staff. But in many instances we have been able to confirm that these factors do not affect our data. In fact, patients may be very quiet on days when the weather is exceedingly unpleasant. If any biometeorological relationship exists, it is a much more complicated one.

Errors due to the presence of one very restless patient in a ward. Undoubtedly the presence of one very restless patient, particularly in the case of mental diseases or asthma, may affect the behaviour of other patients. But, as the total group of patients considered is divided among different wards, different buildings and even different institutes, the effect on the total percentage figures is usually small.

Errors due to differences in sex, age, profession, social status, etc. In many medical and physiological studies the research worker has considered it sufficient to study a particular phenomenon in a few people only, irrespective of their sex, age, profession, social status and other psychosomatic factors. As a result, if the clinical data of groups of people are taken together, an observed increase in complaints among a certain group of people may be offset by a decrease in others. The inference might well be that no relationship exists between the studied clinical phenomena and certain environmental stimuli.

PSYCHIATRIC INSTITUTE ,,HET GROOT GRAFFEL" AT WARNSVELD
Director: Dr. J. Westerhuis

NAME PATIENT: S.W.T. AGE: 46 SEX: M. DIAGNOSIS: Schizophreni

MONTH: november 1960 Name of psychiatrist or head nurse responsible for data: Dr. H.J.P.

Date	6-12 h	12-18 h	18-24 h	0-6 h	Treatment	Remarks
1	R-	R-	R-	OR=		
2	Z.OR. →					
3	OR = →				tranquilizer	P. was very aggressive
4	R -	R+	R +	R +		
5	R-	R-	R+	R+		
6	R+	R+	R+	R+		
7	R+	R+	R+	R+		
8	R+	R-	R-	R+		
9	R+	R+	R+	R+		
10	R-	R-	R-	R-		
11	OR - →				electroshock	P. was throwing plates etc
12	OR = →					
13	OR = →					
14	Z.O.R = →					
15	OR - →			R-		
16	R-	R-	R+	R+		
17	R+	R+	R+	R+		
18	R+	R+	R+	R+		
19	R+	R+	R+	R+		
20	R+	R+	R+	R+		
21	R+	R-	R+	R-		
22	R+	R-	R-	R+		
23	R+	R+	R+	R+		
24	R-	R-	R-	R-		
25	R+	R+	R+	R+		
26	R+	R+	R+	R+		
27	R+	R+	R-	R-		
28	OR = →				tranquilizer	P. was aggresive
29	X →					
30	X →					
31	R-	R+	R+	R+		

LEGEND: Degree of restlessness:

- R = quiet
- OR = restless
- ZOR = very restless
- X = no data

Mood:

- + = good
- ± = changing
- — = bad
- = = very bad

Fig. 32.
Example of daily record sheet of restlessness and mood of mental patients, used for biometeorological analysis.

Please return this form on the 1st day of each month to Dr. S. W. Tromp, Dept. of Internal Medicine, University Medical Centre, Leyden, the Netherlands.

DIAGNOSIS: Bronchial Asthma SEX: male
NAME: G. H. AGE: 34
ADDRESS: de R. str. 26, Amsterdam

MONTH: September YEAR: 1959

DATE	morning 6-12 h	afternoon 12-18 h	evening 18-24 h	night 0-6 h
1	0	0	0	0
2	0	0	0	0
3	0	0	0	0
4	0	0	0	0
5	1	1	1	2
6	1	1	2	2
7	2	2	2	3
8	3 cold wind	3	3	4
9	4 " "	4	4	4
10	4	4	3	3
11	3	2	2	1
12	2	1	0	0
13	0	0	0	0
14	0	0	0	0
15	0	0	0	0
16	0	0	0	0
17	0	0	0	0
18	0	0	0	1
19	1 = tired	1 nervous	1	1
20	1	1	0	0
21	0	0	0	1
22	0	0	2	1
23	1	2	2	1
24	1	0	0	0
25	0	0	0	0
26	0	0	0	0
27	0	0	0	0
28	0	0	0	0
29	0	0	0	0
30	0	0	0	0
31	0	0	0	0

Please indicate in each of these partitions the general state and degree of your asthma, if possible exact hour that your complaints begin or increase.

No complaint = 0; wheezy, usually peeping noise = 1; slightly breathless = 2; breathless = 3; very breathless = 4.

If possible, indicate what you think may be the cause of the attack, *e.g.*, caught a cold, tiredness, sickness, nervousness, difficulties in work or at home, sleepless, menstruation, dusty air.

Please fill in these forms every day and not after a few days because, despite a good memory, you are bound to make mistakes in your accurate recording.

Fig. 33.

Example of daily record sheet used by adult asthmatic patients.

This experience implies that the clinical material should be subdivided into fairly homogeneous groups of patients in every biometeorological study; otherwise the enquiry will be abortive.

Summarizing what has been said we feel that if large, fairly homogeneous groups of patients are taken, the total picture obtained will give us a reasonably satisfactory impression of the average daily fluctuations in complaints of this group despite the many inaccuracies, enabling us to compare these fluctuations with specific weather conditions. On p. 176 we shall discuss the statistical methods which will enable us to confirm or deny the existence of certain correlations deduced from a comparison between weather charts and clinical charts.

Section 3. The Experimental Method

A direct experimental approach to biometeorological problems may be made independently of previous empirical studies, or else it may be a continuation and elaboration of such studies.

Many acclimatization studies (see p. 372), in which a person is subjected to changing temperature and humidity conditions during which a number of physiological factors (such as blood pressure, body temperature, etc.) being continuously recorded, are typical examples of the first type of experimental approach. It is not surprising that until recently workers in this field did not realize that they were studying experimental biometeorology and not just physiology.

Many of these studies are carried out in specially controlled chambers, called *climatic chambers* (also known as *low pressure chambers*), which enable us to control temperature, humidity, air movement, atmospheric pressure, ionization of the air and radiation (infrared, ultraviolet, etc.). On p. 617 J. D. Findlay and J. A. McLean review the general construction and physical principles involved in such climatic chamber studies.

Similar studies are made after previous empirical studies. For example, if in a particular season a change in blood pressure, haemoglobin content and other physico-chemical compounds of the blood has been observed, an observation based on empirical studies of a large group of healthy people of the same sex and age group, one would like to know the deeper causes of this seasonal relationship.

If a weather analysis of these various seasons suggests the influence of certain meteorological factors and a statistical analysis confirms the statistical significance of the observed relationship, one must try to imitate these weather conditions in a climatic chamber in order to see whether the assumed meteorological factors are really responsible for the physiological phenomena mentioned.

In the following chapters many examples of empirical and experimental biometeorological studies will be discussed which will illustrate more clearly the statements above.

Section 4. Statistical Methods to be Used in Biometeorological Research

As pointed out in the previous sections, once it is assumed that a correlation between certain clinical phenomena and specific weather conditions may exist, there are several methods of discovering whether the assumed relationship is due to a chance distribution only or to a highly significant statistical correlation. It should be kept always in mind that even an extremely significant statistical relationship can never "prove" that a relationship really exists. However, experimental work has shown that with a sufficiently high degree of statistical probability an assumed relationship can be accepted as a true one, the more so if specially devised experiments enable us to predict a result and such a result is really obtained each time the experiment is repeated.

Because of the great biological differences even between individuals of the same species, sex and age group, practically all the so-called "facts" in biological sciences are based on statistical evidence only; in other words, a given result of an environmental stimulus can be expected in "most" experiments but not necessarily in every experiment. This applies to physiological, pharmacological tests and the like.

At the beginning of the 20th century biological and medical scientists tended to neglect statistical analysis of the results obtained. At present they seem to have gone to the other extreme: if a result cannot be confirmed statistically, it is automatically rejected as not being true.

Both extremes lead to erroneous results, of course. It should be realized that for many complex biometeorological phenomena even the most competent statistician is not able to develop a formula for testing the reality of a relationship found graphically. What might be called an "automatic" statistical analysis performed by statisticians inadequately trained in biology and physiology has too often been practised as the result of an excessive respect for statistics.

One should never forget that a statistical analysis of a relationship with average temperature, fronts, air masses, etc. assumes that each of these factors is mathematically the same. Also, it is assumed that the same front or temperature interval will always produce the same physiological result. Neither of these assumptions is true. First of all, as we have seen, there are cold and warm fronts but each also differs in its degree of activity (see p. 82). According to Wilder's Law (see p. 199), which is true for single cell and nerve stimulation but also for more complex physiological processes, the same external stimulus may create an entirely different result, depending on the previous history of the stimulated object (for further details see p. 199). A similar phenomenon is known in the inorganic world if a force, exceeding the internal limit of elasticity of a body, causes a small permanent (plastic) change in the body. Whereas no outer difference in the result of the stimulating external force is observed after a number of stimuli, at a certain moment, when the internal micro-sliding planes reach the surface, a crack will develop and two parts of the body will move relative to each other, although the external force has remained the same. In organic life this phenomenon is more common and the effects show up more drastically.

It is evident from these facts that a statistical analysis of biometeorological data which does not take these facts into consideration, is bound to lead to entirely negative results, as has so often happened in the past.

In all modern textbooks on biological or medical statistics the student of biometeorology can find the various methods and formulas to be used for statistical analysis. We shall not repeat all these methods in this Section, but we should like briefly to discuss some useful methods which have been used very successfully in biometeorology and which can be recommended to biometeorologists not specially trained in mathematics. For further details I recommend the reader to refer to the publications of Berg[447, 448], De Rudder [449, 450] and von Schelling[453-455].

Before some of the important statistical methods and formulas are discussed, I should like to refer to an *empirical method* described by Berg[448] in 1957, which may provide a solution in those cases where ordinary mathematical statistics fail to give an answer to the problem. The geographical distribution maps of cancer of the lung in the Netherlands will be enlisted (Fig. 34) to demonstrate this method. This map was prepared along the lines described above. It clearly shows a high mortality in the three Western Provinces (Utrecht, S. Holland, N. Holland) and in the S.E. parts of the Province of N. Brabant. It is necessary to find out statistically whether this distribution is significant or only a chance distribution. However, the different sizes of and numbers of the population in the various municipalities, the unequal number of municipalities in the different mortality frequency groups, etc., are factors which make a normal statistical analysis difficult, if not impossible. Berg suggested the following procedure. The differently coloured municipalities are represented by similarly coloured small balls. If there were 50 black municipalities, 50 black balls were selected, 80 green municipalities are represented by 80 green balls and so forth. All these balls, representing approximately 1000 municipalities, are thrown together and thoroughly mixed. One person points to a municipality and another blindly draws a coloured ball out of the box. If it is blue, that municipality is given a blue colour. By doing this for all municipalities, a coloured map is obtained (see Fig. 35). Figs. 34 and 35 are significantly different. Berg suggested a special X^2-test to demonstrate the degree of difference between both maps (see ref.[448, p. 5]) by putting a grid over the map.

A similar analysis can be made of a graph representing, say, the daily percentage of restless patients in a constant group of mental patients. Three hundred and sixty values of one year of observations can be put on small pieces of paper or balls which are thoroughly mixed. The balls are drawn blindly, the first ball represents the first day of the year, the second one the 2nd day, etc. By using the percentage figures indicated on each ball, a random percentage curve can be made, which should deviate significantly from the curve actually observed.

Fortunately, in many other instances the regular statistical methods can be used. Before doing this, however, a graph should first be made of the various data collected. Some correlations are very often overlooked if a mathematical calculation is made automatically.

The various steps to be taken can be summarized as follows:

The standard deviation

After the clinical data are represented in a graph, indicating, for example, the daily variation in percentage of complaints, mortality, etc., the monthly average can be determined. The part of the curves above this average is indicated in black (see asthma curve, Fig. 84). As some of the peaks above the average may be due to a chance fluctuation, it is necessary to ascertain statistically how far a peak in the curve should rise above the monthly average before it can be accepted as a significant deviation. For this purpose the *standard deviation* (σ) has to be determined.

If n observations of a quantity are $X_1, X_2 \ldots X_n$ and their average is $\bar{X}$, defined by $n\bar{X}$ = sum of the individual observations, the "standard deviation" is defined as follows:

$$n^2 = (X_1 - \bar{X})^2 + (X_2 - \bar{X})^2 + \ldots (X_n - \bar{X})^2$$

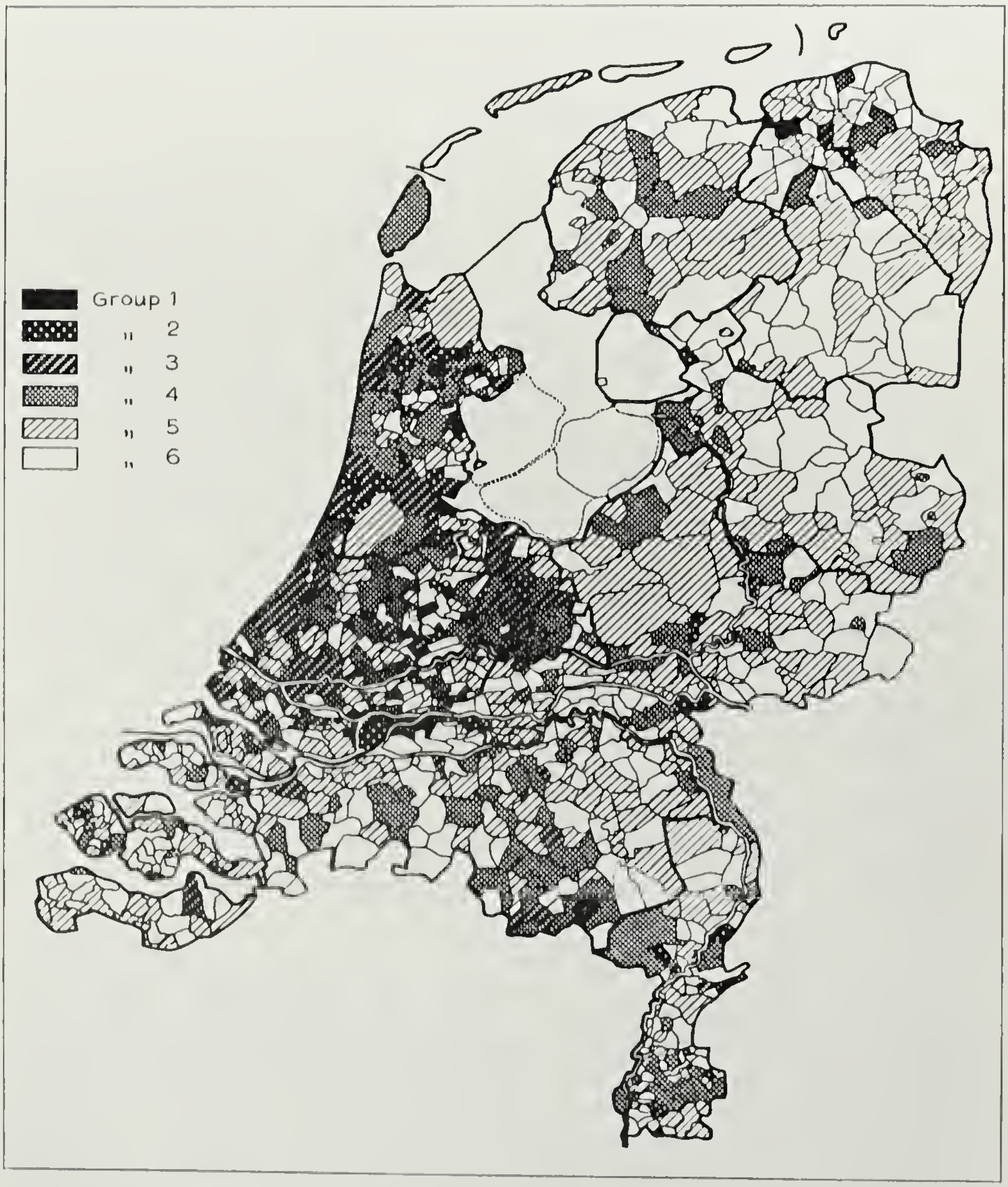

Fig. 34.
Geographical distribution of lung cancer mortality in the Netherlands in the male population above the age of 50 years (period 1936-1952) based on data of the Netherlands Central Bureau of Statistics, compiled by S. W. Tromp. Observed distribution.

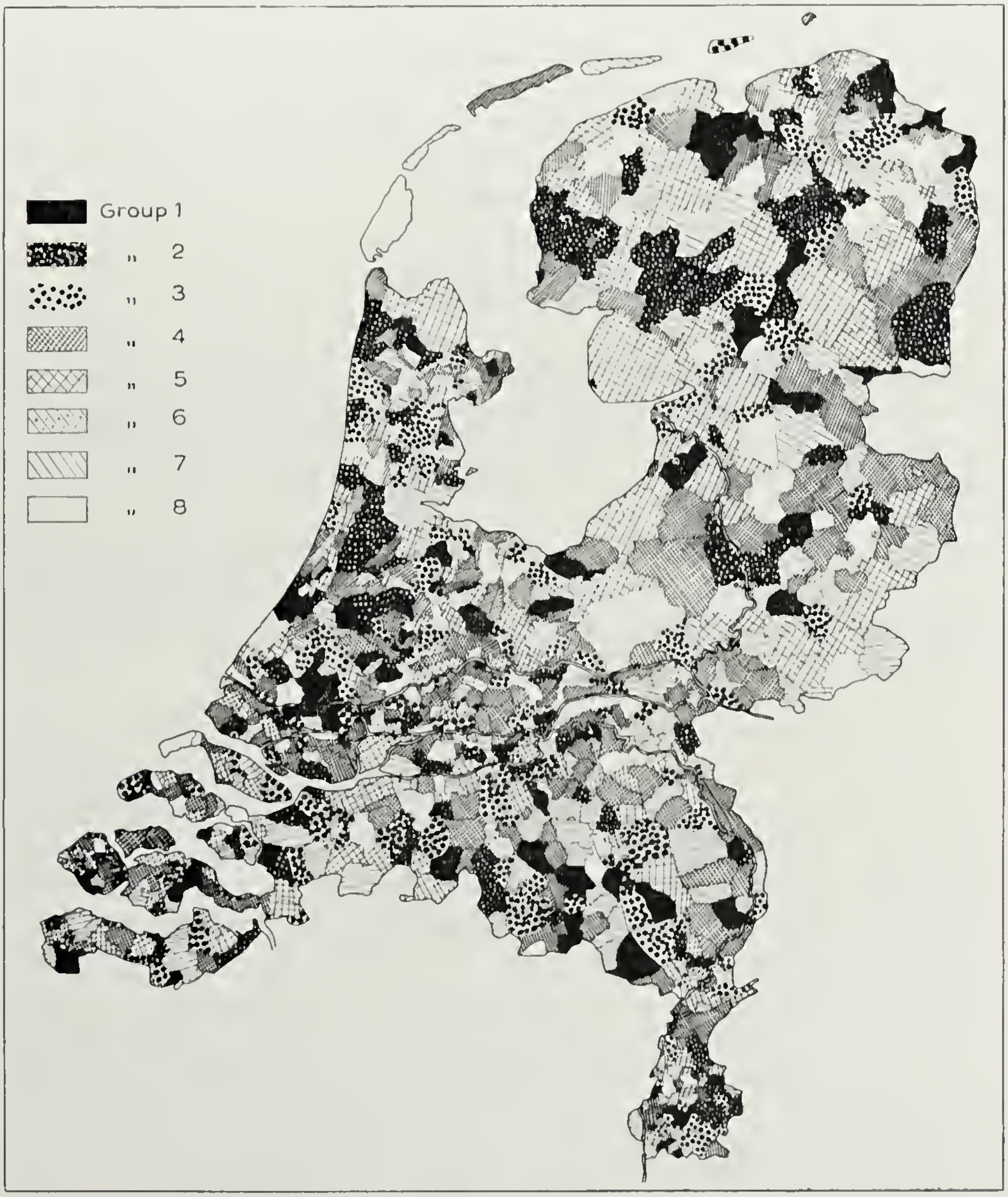

Fig. 35.
Geographical distribution of lung cancer mortality in the Netherlands in the male population above the age of 50 years (period 1936-1952) based on data of the Netherlands Central Bureau of Statistics, compiled by S. W. Tromp. Random distribution.

Usually the "standard deviation" is calculated on the assumption that the mean of the sample of observations available is the true average of the element. This is not always correct. The average depends on the number of observations. In order to minimize this source of error the sum of squares of departures is not divided by n but by $n - 1$. The formula for the standard deviation is therefore as follows

$$\sigma = \sqrt{\frac{(X_r - \bar{X})^2}{n - 1}}$$

in which $X_r - X$ represents the difference between each observed value and the total average, known as the *departure*. The sum (Σ) of the squares of these departures must be divided by the number of observations minus 1. The formula using the value $n - 1$ is often termed the *standard error* of the sample.

All observed values in our clinical curves which exceed the monthly average by twice the "standard error" have a 95% chance of being true departures from the normal; 2.58 times the standard error represents a 99% probability, 3.19 σ indicates a 99.9% probability.

Progressing averages

If curves are very irregular, it is customary to "flatten" the peaks by using the so-called "*progressing averages*". For example, if the daily percentages 10%, 12%, 18%, 8%, 16%, 15% etc. are plotted in a graph, the average value of each 3 numbers could be taken $(10+12+18)/3$, $(12+18+8)/3$, etc. and these averages are plotted, making the curve more smooth.

The run test

In a curve representing daily variations in complaints from a disease (*e.g.* number of patients having an asthma attack) we often find an accumulation of high or low figures, called *runs*, which often make a statistically significant impression but which may be entirely due to a chance distribution. A fairly simple, but usually trustworthy, test to analyse such a curve is known as a *run test.*

The test consists of the following procedures:

(1) First the various observed values (*e.g.* mortality figures, daily percentages of certain complaints) are classified from low to high and next to each value the number of times that this particular value is observed in the curve is noted.

(2) A median line is drawn through this series of values in such a way

that almost the same number of occurrences can be found above and below this line. For example, only the values 0–7 were observed with the following frequencies 0(4×), 1(5×), 2(6×), 3(6×), 4(5×), 5(5×), 6(0×), 7(1×). The median line lies between 2 and 3 because 4+5+6 equals roughly 6+5+5+1. The values above this median line are indicated by the "plus" sign and those below by a "minus" sign.

(3) We return to the row of figures actually observed, *e.g.* *022102* 75747 *221*. The first 6 and last 3 figures are positive runs, the group 75747 is a negative run. The total number of positive runs in a curve is indicated by m_1, the negative runs by m_2. In this example $m_1 = 2$, $m_2 = 1$.

(4) In order to know whether these runs differ significantly from a chance distribution, the following formula is used:

$$T = \frac{R_o - R_e}{\sigma}$$

if R_o = observed number of runs, R_e = expected number of runs, σ = standard deviation.

R_e is calculated with the formula:

$$R_e = \frac{2m_1m_2}{n} + 1$$

in which $n = m_1 + m_2$.

σ is determined by means of the formula:

$$\sigma = \sqrt{\frac{2m_1m_2\,(2m_1m_2 - n)}{n^2\,(n - 1)}}$$

If $T \geqq 2$, there is a 50% probability that the run distribution is due to chance only. If $T \geqq 2.6$, there is a 1% probability and if $T \geqq 3.2$, there is only 0.1% probability. This method should only be used if the number of figures is large enough, *e.g.* around 40 or more.

The integral of probability of Gauss

(1) In order to determine whether the number of cases of a certain disease or physiological phenomenon observed on days, when special meteorological conditions prevail, exceeds the number which can be expected on grounds of chance probability only, the *integral of probability of Gauss* is often applied:

$$I.P. = \frac{Z_n - \dfrac{n \cdot Z_N}{N}}{\sqrt{\dfrac{2 \cdot n \cdot Z_n}{N} - \left(1 - \dfrac{n \cdot Z_N}{N^2}\right)}}$$

in which N = total number of days or hours during which the biometeorological relationship between weather element and certain clinical phenomena have been studied, n = number of days with a specific meteorological pattern, *e.g.* days with cold-front passage, polar air influxes, steeply falling temperatures or great atmospheric turbulence, etc., Z_n = number of times when on these n days a certain clinical or physiological event is observed, *e.g.* a rise in frequency of asthma attacks or rheumatic complaints within 24 hours after the passage of a cold front; a similar rise in blood pressure, etc., Z_N = total number of cases of the same phenomena observed during the whole period of N days.

If $I.P.$ exceeds 2.1 there is a 99.73% probability.

Example. During 1956 in the Netherlands, in a constant group of asthmatic children, the daily percentage of children with asthma attacks was recorded. In this case N was 366 days, n = number of days with cold front passages = 87, Z_n = number of times that an increase in asthma attacks was observed within 24 hours of the passage of a cold front = 59, Z_N = the number of times in 1956 when a day was followed by a day of increased asthma attacks = 142.

If these values are introduced into the Gauss' formula it is found that $I.P.$ = 3.22; in other words, that there exists a highly significant statistical relationship between cold front passages and increase in asthma attacks.

(2) Another method of determining the statistical significance of an observed biometeorological relationship between weather elements and certain clinical phenomena is the *T-method* devised by von Schelling[153-155]. In this method the observations are split up as in Table 24. In von Schelling's formula

$$T = (a_1 \cdot b_2 - a_2 \cdot b_1) \sqrt{\frac{N - 1}{c_1 \cdot c_2 \cdot A_1 \cdot A_2}}$$

If $T > 2$ (according to the statistical tables of Fisher and Yates) a 96% probability can be expected. If $T > 3$ a 99.73% probability can be expected.

(3) A third method, which is often used in biometeorology, is known as the *n-method*[150] or *synchronization method*. It was developed in 1933 by G. Ortman[152] and independently of him by T. and B. Düll, being elaborated in 1935 by M. Gundel and O. Hoelper. In this method a table is prepared as indicated below (Table 25). The left column gives the dates of days when there was a specific meteorological disturbance (so-called n-days), *e.g.* passage of fronts. The dates when a certain clinical phenomenon occurs are given in the second column. The pathological dates may coincide with the n-dates or they occur one or two days earlier (indicated as n — 1 or

TABLE 24

	Days (or hours)		Total
	with a specific meteorological disturbance	*without a specific meteorological disturbance*	
Number of days (or hours)	a_1	a_2	$c_1 = a_1 + a_2$
Number of days (or hours) with a certain pathological or physiological phenomenon during:	b_1	b_2	$c_2 = b_1 + b_2$
Total	$A_1 = a_1 + b_1$	$A_2 = a_2 + b_2$	$N = c_1 + c_2 = A_1 + A_2$

$n - 2$) or 1 or 2 days later ($n + 1$ or $n + 2$ days). It should be borne in mind that there should be an interval of at least four days between 2 successive n-days before such an analysis can be made.

The *synchronous* days are recorded in the four columns on the right-hand side of the table; *i.e.*, an entry is made to show whether the clinical phenomenon occurred one or two days before or after a certain date when special weather conditions prevailed.

TABLE 25

Dates of meteorologically disturbed days	*Dates of occurrence of certain clinical phenomena*	*Number of synchronous days*				
		n—2	*n—1*	*n*	*n+1*	*n+2*
1 December	3 December					1
10 December	9 December		1			
25 December	26 December				1	
etc.	etc.			etc.		

If in the example given the meteorological event occurred on both 1st and 2nd December, the pathological event of 3rd December should be marked in column $n + 1$ as well as $n + 2$.

In the event of a significant statistical relationship, a concentration of lines is observed in one of the columns. Von Schelling[453–454] developed a special method in 1938 by which to determine whether this is due to chance only.

The total number of marks is determined for each of the n columns individually. The greatest difference between these values observed in two

n columns ($= d$) should be at least f times the differences observed between the other n-columns before a significant statistical correlation can be accepted, in other words

$$d > f\,\sigma_d \quad \text{in which} \quad \sigma_d = \sqrt{\frac{2N}{R}}$$

fi N = total number of marked pathological synchronous days, R = number of n columns (in our example only 4 were given but one could also compare the clinical data with a weather date 5 or more days ago or afterwards), f = factor depending on R. According to von Schelling the following significance values can be calculated for f:

$R = 2$	$f = 3.0$	$R = 12$	$f = 3.67$
$R = 3$	$f = 3.20$	$R = 13$	$f = 3.69$
$R = 4$	$f = 3.32$	$R = 14$	$f = 3.71$
$R = 5$	$f = 3.40$	$R = 15$	$f = 3.73$
$R = 6$	$f = 3.46$	$R = 16$	$f = 3.75$
$R = 7$	$f = 3.51$	$R = 17$	$f = 3.76$
$R = 8$	$f = 3.55$	$R = 18$	$f = 3.78$
$R = 9$	$f = 3.59$	$R = 19$	$f = 3.79$
$R = 10$	$f = 3.62$	$R = 20$	$f = 3.80$
$R = 11$	$f = 3.64$	$R = 21$	$f = 3.82$

It should be remembered that the n-method can only be used to test the significance of certain "cases" (*e.g.* number of heart attacks, poliomyelitis cases, etc., on certain days) but should not be used for direct laboratory measurements such as number of leucocytes, blood pressure values, etc., recorded on certain days.

We should like to confine ourselves to these few methods which have proved to be of great practical value in biometeorological studies. For more complex problems bioclimatologists are strongly recommended to request the assistance of experienced biostatisticians, as otherwise serious statistical errors are liable to be made.

In the previous three Parts a brief review has been given of some of the most important meteorological and climatological aspects of biometeorology, which will facilitate the discussion of the following chapters. On p. 447 some of the basic physiological processes in the human body will be reviewed, which is essential for a clear understanding of the interaction between the atmospheric environment and the human body.

PART IV

Effect of Weather, Climate and Season on Man

CHAPTER I

Biometeorological Effect on Healthy Man (Physiological Biometeorology)

Since Claude Bernard and Walter Cannon introduced the concept of constancy of internal environment, known as *homeostasis*, which assumes that the coordinated physiological processes will maintain most of the steady states in the organism, physicians and physiologists are inclined to consider the processes in the human body as fairly static.

This concept has also tended to lead epidemiologists to consider the human body, or a population group as a whole, as a fairly constant, unchanging unit, the cause of epidemics being mainly due to changing environmental conditions which are assumed to favour the development of certain bacteria or viruses or to affect the contact facilities between people or between a person and the infective agent.

Biometeorology, more than any other science, has been able to demonstrate that the physiological processes in the human body are constantly changing owing to changes in climate and weather. As a result, the general pathological resistance of the human body varies from day to day, through the year and from one year to another.

The word *stress*, introduced into medical science notably by H. Selye, at present Director of the "Institut de Médecine et de Chirurgie expérimentales" at the University of Montreal in Canada, will often be used in the following chapters.

In this book it will be used to designate an excess of nervous strain on the various endocrinological and nervous systems imposed by usually strong or prolonged stimuli set up by changes in the environment, a strain to which the physiological mechanism of the human body cannot easily adapt itself and which prevents or counteracts the condition of homeostasis. In the field of biometeorology one usually speaks of *climatic* or *meteorological stress*.

As we hope to show in the following chapters, the same meteorological factor (or group of factors) seems to have a triggering effect on a number of entirely different physiological or pathological processes in the human body. This observation suggests that the principal point of attack of meteorological agents must be located in certain organs which control a great number of physiological processes. Accumulated evidence suggests that in all probability meteorotropism operates mainly through the hypothalamus, the autonomic nervous systems and the ductless glands (esp. the pituitary, thyroid and adrenal gland). The functioning of these various organs is fully described in the various textbooks of physiology and in a great number of specialized journals, often difficult of access to the non-specialist in physiology.

In Parts I–III a summary is given of only those meteorological data which are of direct importance to the student in biometeorology. For the same reason, only those physiological processes will be described in this Part which are of special importance to the study of biometeorological phenomena. A thorough understanding of these physiological mechanisms will greatly help the reader to follow a brief descripton and explanation of the various meteorotropic phenomena to be discussed in the following chapters.

Section 1. Brief Review of those Physiological Processes in Man which are Important from a Biometeorological Point of View

In the following section a choice had to be made between the many physiological phenomena of interest to the biometeorologist. Only those aspects have been reviewed that are related to the various subjects which have been studied in biometeorology during the last 50 years and which may assist the reader to understand the observed biometeorological relationships.

For practical purposes the physiological phenomena to be discussed have been classified into the following main groups:

A. Functioning of the autonomic nervous systems.
B. Functioning of hypothalamus and thalamus.
C. Thermoregulation.
D. Functioning of ductless glands.
E. Functioning of spleen, liver and gall bladder.
F. Breathing mechanism.
G. Highest control centres of the brain.
H. Factors affecting the composition and physico-chemical state of the blood; 17-ketosteroid secretion; diuresis; capillary resistance and permeability of membranes.
I. Influence of solar radiation on health and disease.
J. Influence of air ions on certain physiological functions.
K. Biological rhythms.

Subsect. A. FUNCTIONING OF THE AUTONOMIC NERVOUS SYSTEMS

1. *General Mechanism*

In order to facilitate the reading of the following sections by the non-physiologically trained reader, a few generally known anatomical details will be given, which are further explained in the Figs. 36–41. The student of biometeorology is particularly recommended to study in detail the excellent atlas of the nervous system by Frank H. Netter, published by Ciba Pharmaceutical Products, Inc., since 1953.

Every nervous system is composed of nerve cells, known as *neurons,* 4–100μ large, globular, pear- or spindle-shaped cell bodies composed of protoplasm with many fibres, nucleus, etc. From each neuron numerous short processes extend, the *dendrites* (ramified protoplasmatic offshoots) and one long fibre, the *neurite* or axon, which is a branched protuberance of the nerve cell. The branches of this axon are called collaterals.

A number of neurites, each surrounded by connective tissue, form the nerve fibres; they are grouped together in nerve bundles (like submarine cables) and create the actual nerve, divided into myelinated and unmyelinated nerves, depending on whether the neurite is covered by a thick viscid insulating layer called myelin, composed of certain proteins, or not.

Most nerve cell bodies are grouped together in segmentally arranged masses, known as *ganglia.* They are called *post-ganglionic* when the ganglion is located outside the central nervous system (see later) and *pre-ganglionic* when the cell bodies are located in the central nervous system. Points of contact between individual neurons are called *synapses,* the junction being generally formed by multiple points of contact. Many axon collaterals terminate in *end-plates,* swellings which are applied to the surface of both dendrites and cell bodies of other neurons*.

The actual physico-chemical mechanisms involved at the synapses and end-plates are not known with certainty. However, it is very likely that in many instances at least the transmission at a neuro-myal junction takes place through liberation of specific chemical mediators such as *acetylcholine,* an active ester of *choline,* $CH_2(OH){\cdot}CH_2N(CH_3)_3OH$, and *sympathin.* The transmission is affected by various physico-chemical conditions, *e.g.* fluctuations in the potassium and calcium content and acidity of the environment of the ganglia. The acetylcholine is rapidly destroyed through hydro-

* Eccles, Konorski and Young (see p. 242) demonstrated that prolonged disuse of synapses leads to defectiveness of synaptic function, whereas repetitive stimulation increases the functional efficiency. The size of neurons and dendrites depends on the amount of afferent influences that falls upon them.

Fig. 36. Medial aspect of the brain.

A.C. anterior commissure; A.P.S. anterior parolfactory sulcus; C. cuneus; Ca.F. calcarine fissure; C.F. body of fornix; C.P. cerebral peduncle; C.P.V. 3 choroid plexus of 3rd ventricle; Co.F. column of fornix; D.F.H. dentate fascia of hippocampus; F.G. fusiform gyrus; F.I. interpeduncular fossa; G.C. gyrus cinguli; G.C.C. genu of corpus callosum; H.G. hippocampal gyrus; I.T.G. inferior temporal gyrus; L.G. lingual gyrus; L.Q. lamina quadrigemina; M.I. massa intermedia; M.B. mammillary body; O.C. optic chiasm; O.R. optic recess; P.A. parolfactory area; P.C. precuneus; P-C. posterior commissure; P.O.S. parieto-occipital fissure; P-C.L. paracentral lobe; Pi. pineal body; Pit. pituitary gland; P.P.S. posterior parolfactory sulcus; R.C.C. rostrum of corpus callosum; S.C. sulcus cinguli; S.C. (P.F.) sulcus cinguli (pars frontalis); S.C. (P.M.) sulcus cinguli (pars marginalis); S.C.C. splenium of corpus callosum; S.C.G. subcallosal gyrus; S.F.G. superior frontal gyrus; T.C.C. trunk of corpus callosum; Th. thalamus; T.P. temporal pole; U. uncus.

(from: Frank H. Netter, *The Ciba Collection of Medical Illustrations, Vol. 1, Nervous System,* 1958, p. 40)

lysis by an enzyme, *cholinesterase,* which is present in tissues and blood. Cholinesterase is inhibited by *eserine.*

Towards the central nerve organs in the body the nerves unite into larger bundles. Two main centres of nerve control are distinguished,

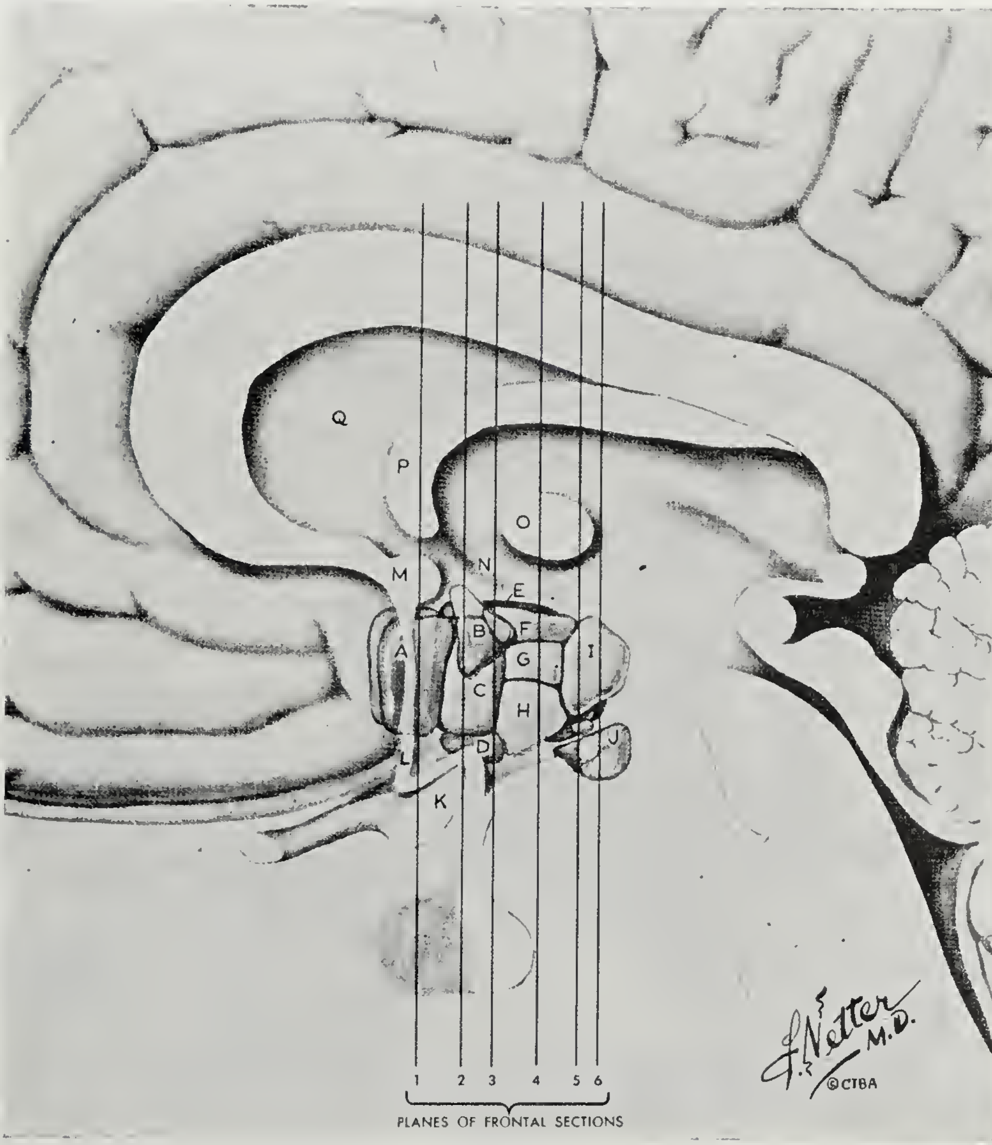

Fig. 37.

General topography of the hypothalamic area, also known as diencephalon. A: preoptic nuclei; B: paraventricular nucleus; C: anterior hypothalamic area; D: supra-optic nucleus; E: lateral hypothalamic area; F: dorsal hypothalamic area; G: dorsomedial nucleus; H: ventromedial nucleus; I: posterior hypothalamic area; J: mammillary body; K: optic chiasma; L: lamina terminalis; M: anterior commissure; N: hypothalamic sulcus; O: intermediate mass of thalamus; P: fornix; Q: septum pellucidum. (from: Frank H. Netter, *The Ciba Collection of Medical Illustrations, Vol. 1, Nervous System*, 1958, p. 147)

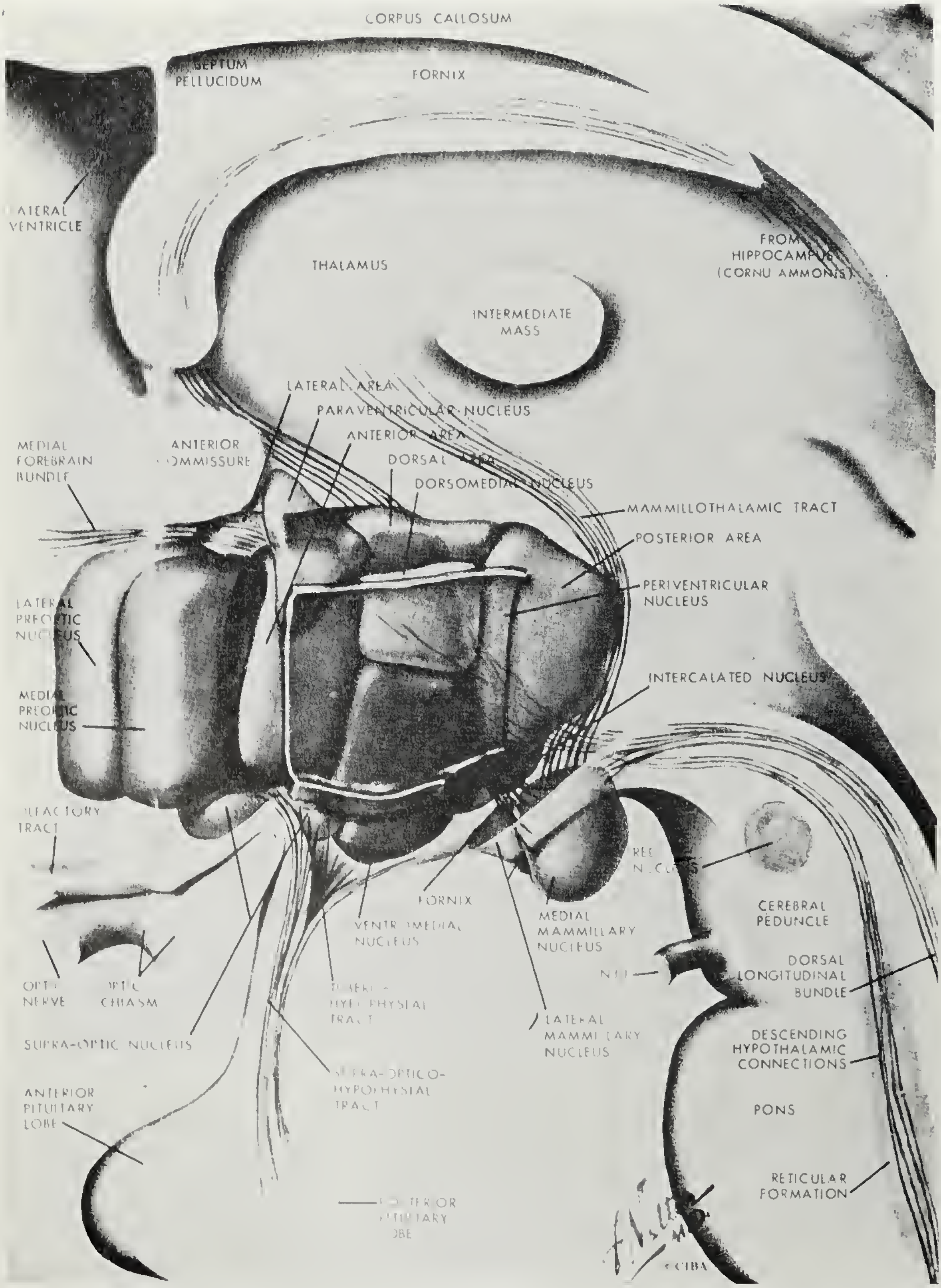

Fig. 38.
Schematic, three-dimensional reconstruction of the hypothalamus. (from: Frank H. Netter, *The Ciba Collection of Medical Illustrations, Vol. 1, Nervous System*, 1958, p. 151)

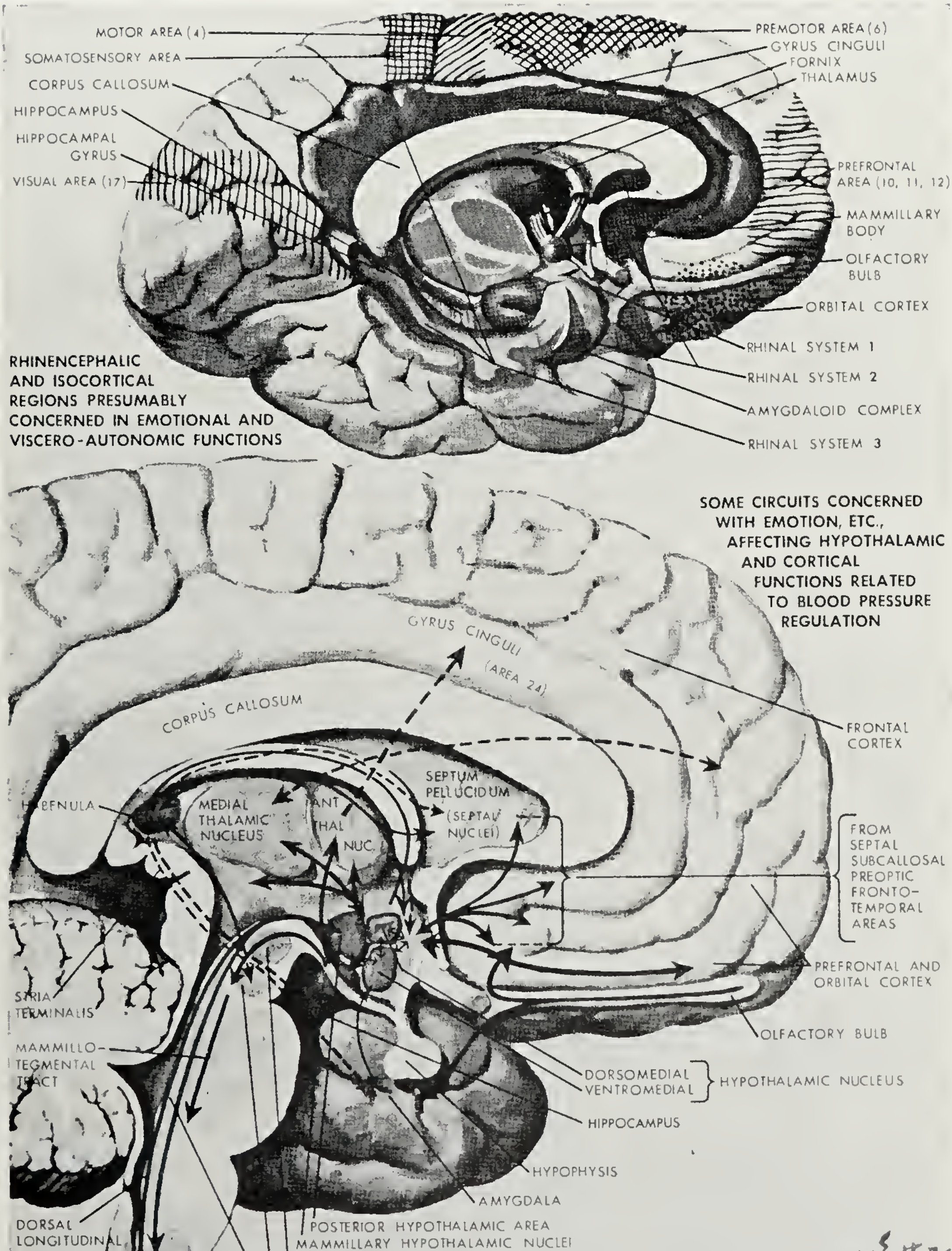

Fig. 39
Cerebral regions associated with the hypothalamus. (from: Frank H. Netter, *The Ciba Collection of Medical Illustrations, Vol. 1, Nervous System,* 1958, p. 152)

the *animal* or *central nervous system* and the *autonomic* or *involuntary nervous system.*

The animal or central nervous system

This organ regulates our psychic processes and conducts consciously perceived phenomena controlled by our volition, such as movement, etc. It is composed of the spinal marrow, its continuation in the skull *(medulla oblongata),* the further extension into the brain, and the nerves connecting these central parts with the various organs.

The brain comprises two main parts (see Figs. 36 and 39), *viz.,* the *cerebrum,* also known as *telencephalon,* (covering $^7/_8$ of the upper part of the skull) and the *cerebellum* (situated behind the cerebrum and above the pons, see below). The cerebrum is separated by a deep grove into two hemispheres; the outer layer, the cerebral *cortex* (the centre of our sense organs), consists mainly of grey matter and is composed of a group of nuclei. On the floor of the groove, between the two hemispheres is the *brainstem.* Both hemispheres are connected by the *corpus callosum,* the great commissure system (connecting bands of tissue) of the cerebrum. The actual connection between brainstem and both hemispheres is formed by a group of perforations known as the *foramina Monroi.*

The brainstem is usually classified from the front towards the rear into four parts: the *diencephalon,* the *mesencephalon,* the *pons Varoli* (connecting the cerebrum, cerebellum and medulla oblongata) and the *medulla oblongata* (see above).

The cerebellum represents the roof of the pons Varoli and medulla oblongata. It is connected by three pairs of brachia (arms) with the brainstem: the brachia conjunctiva, the brachia pontis and the corpora restiformia.

In a cross section of the diencephalon the following anatomical units can be distinguished:

(1) The roof part, known as *lamina epitheliasis* and consisting of a very thin layer of a thickness of one cell only. Both structurally and functionally it is connected with the plexus chorioideus (vascular coat of the eye) and plays an important role in the formation of the liquor cerebrospinalis.

(2) The lateral (side) parts of the diencephalon, consisting of a dorsal part, known as *thalamus opticus* (a large ovoid mass), consisting chiefly of gray matter, which is a very important sensory centre, see p. 205, and two ventral parts. These two downward directed lateral parts of the diencephalon are connected by a basal plate and form together the *hypothalamus* (Figs. 36–39).

The hypothalamus consists of four main parts which are indicated, from the front towards the rear, as *area preoptica* (the telencephalic or cerebrum part of the hypothalamus), *area supra-optica, tuber cinereum* and the *pars mammillaris* (Fig. 37).

Within these boundaries are clusters of cells known as *hypothalamic nuclei* (see p. 202), which are classified from the front towards the rear into the *anterior nuclei* (supra-optic, paraventricular and infundibular nuclei), the *middle nuclei* which occupy the middle part of the tuber cinereum (ventromedial, dorsomedial and lateral hypothalamic nuclei) and the posterior nuclei which consist of the mammillary-infundibular nuclei, the *posterior part* of the tuber cinereum and the medial and lateral nuclei of the mammillary body.

The posterior part of the tuber cinereum functions as a supernuclear orthosympathetic regulation centre, whereas most of the anterior nuclei are responsible for parasympathetic regulation (see below)*.

The autonomic or involuntary nervous system

It is composed of two strings, the peripheral ganglia, situated on either side of the spinal column, the ganglia of each chain being connected by longitudinal fibres. The lateral ganglia send post-ganglionic fibres to the spinal nerves, which convey sympathetic post-ganglionic fibres to the bloodvessels, sweat glands, smooth muscle, intestines, etc.

The autonomic (involuntary) nervous system has recently been classified into three (not two as in the past) main systems, the great significance of the third having only latterly been fully appreciated. These systems are known as the orthosympathetic, parasympathetic and peripheral nervous systems (Figs. 40 and 41).

(1) The *orthosympathetic nervous system,* also known as *sympathetic nervous system proper,* consists of the connector cells, the fibres, ramifications and excitor neurons** of the thoracic region and of the first two lumbar segments of the spinal cord. Stimulation of the nervous system enables the organism to adapt itself quickly to sudden changes in the environment.

(2) The *parasympathetic nervous system* consists of the connector cells,

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* I wish to avail myself to this opportunity of thanking Prof. J.J.G. Prick for his guidance in the sections on the neuro-anatomy of the brain and Ciba Pharmaceutical Products Inc. for permitting me to reproduce the figures 36–41 by Frank H. Netter, M.D.

** In the somatic spinal reflex arc three types of neurons are distinguished: the afferent or *receptor* neuron with its cell body in the posterior root ganglion; the *connector* neuron, the cell in the posterior horn of grey matter, which by means of its axon transmits the impulse to the anterior horn; the *excitor* neuron, the anterior horn cell and its axon, which transmits the efferent impulses to a voluntary muscle.

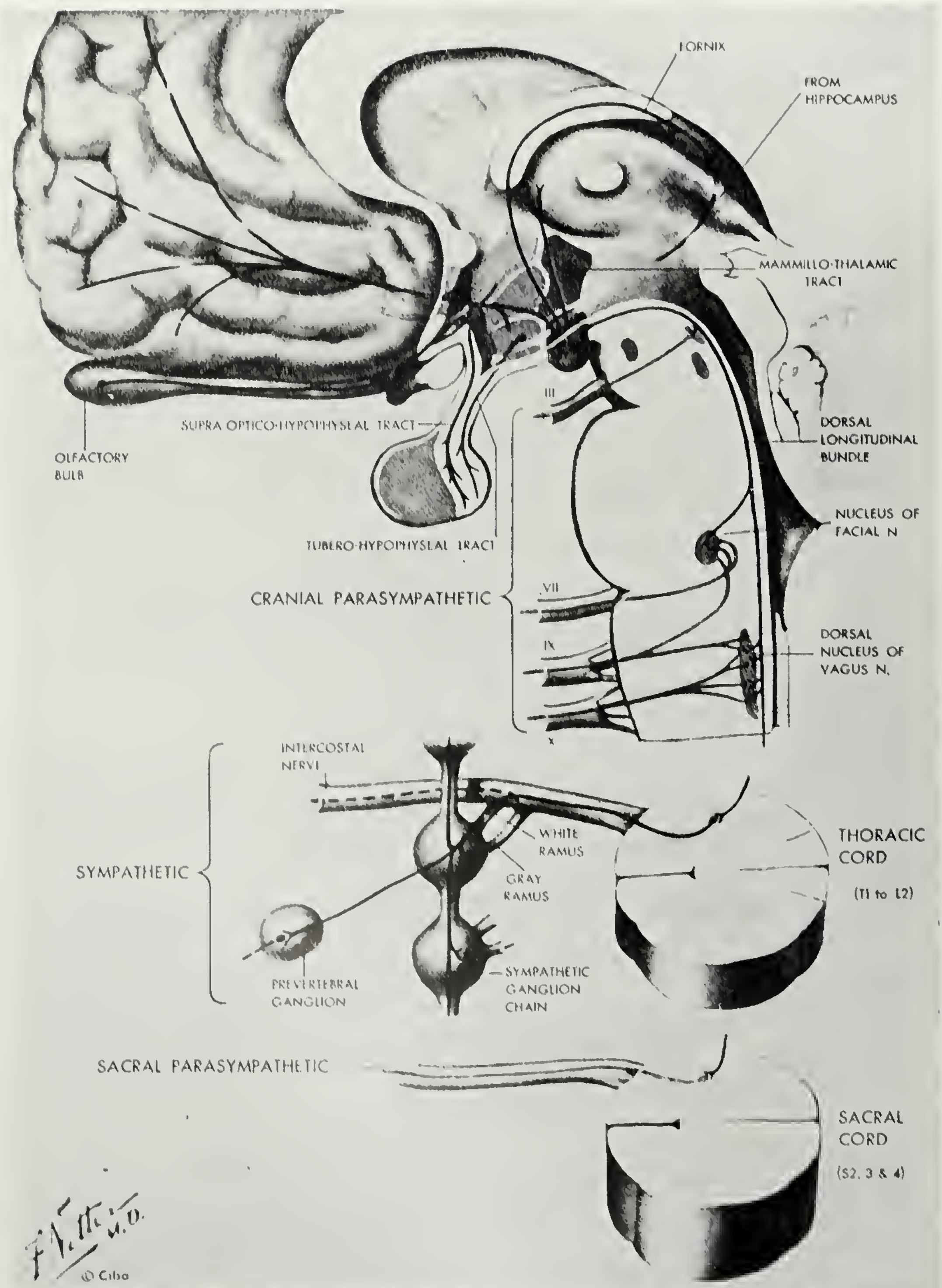

Fig. 40.
Autonomic nervous systems and the afferent and efferent connections with the hypothalamus. (from: Frank H. Netter, *The Ciba Collection of Medical Illustrations*, *Vol. 1*, *Nervous System*, 1958, p. 77)

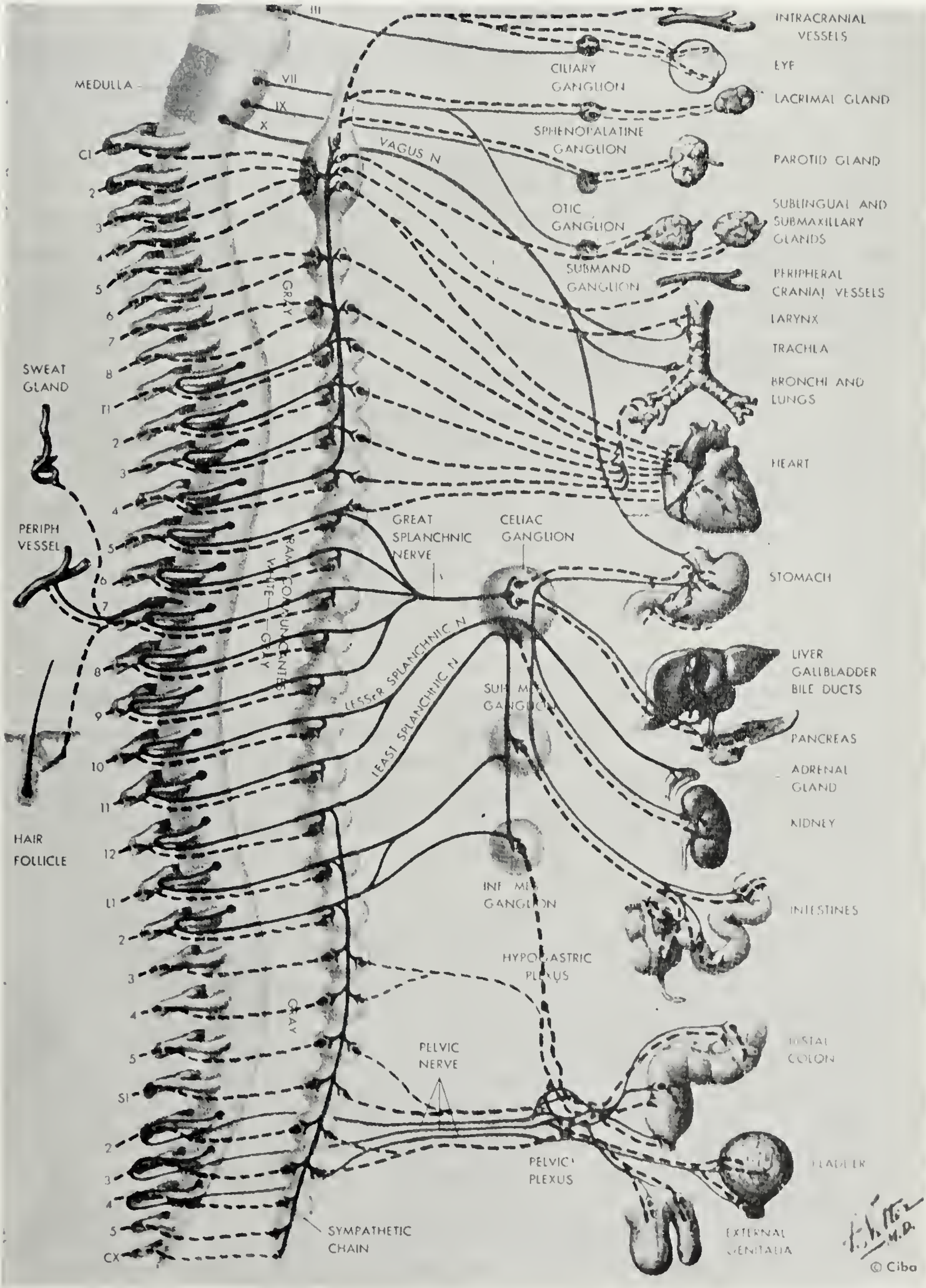

Fig. 41.
The autonomic nervous systems and their control of various organs. (from: Frank H. Netter, *The Ciba Collection of Medical Illustrations, Vol. 1, Nervous System*, 1958, p. 81)

their fibres and related excitor neurons located in the brain (called *cranial division*) and in the second and third sacral segments of the spinal cord (*sacral division*). The principal function of this system is the regulation and recovery of the disturbed physiological equilibrium of the organism as a result of environmental disturbing factors.

Both sympathetic nervous systems are rather antagonistic in their actions on organs which they both supply (*e.g.* heart, bronchi, pupil, etc.)*. Some organs are innervated by one division only: *e.g.* uterus, adrenal medulla and most arterioles by the orthosympathetic system only; glands of stomach and pancreas by the parasympathetic only.

There is usually also a difference in distance between excitor cell and the organ to be innervated: with orthosympathetic stimulation the distance is usually relatively large, whereas in parasympathetic stimulation the excitor cells are, as a rule, in close proximity to the organs.

Another difference is that, when stimulated, the sympathetic post-ganglionic fibres liberate, peripherally, a substance identical with adrenaline. Similar para-sympathetic fibres liberate acetylcholine. However, all the pre-ganglionic fibres (in both nervous systems) liberate acetylcholine at their ganglia.

Adrenaline and acetylcholine have entirely different physiological effects.

Adrenaline causes dilatation of the pupil and retraction of the lids; it accelerates and increases the force of the heartbeat; it increases the excitability of the heart; it increases the blood pressure; it causes constriction of arterioles and capillaries in the skin and of the vessels controlled by the splanchnic nerves (abdominal area), but causes dilatation of vessels in heart and skeletal muscles; it relaxes the muscle wall of the bronchi but increases

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* As pointed out by E. M. Glaser[630] and others, the terms "vagotonia" and "sympathicotonia", often used in older physiological literature, should be discarded, as the two conditions are not necessarily opposed. It should be borne in mind, moreover that a certain physiological phenomenon, apparently typical for orthosympathetic stimulation, could also be the result of a sudden diminution of parasympathetic tonus and *vice versa*. Still, it does not seem to be correct to deny the existence of these two separate autonomic systems as has been suggested in recent years by certain physiologists. It is true that the antagonism between the two systems is less pronounced than we may have thought in the past, but anatomical, histological and histochemical studies have confirmed the existence of both systems (Meyling[524, 525]) *e.g.* by using the histochemical colour tests devised by Champy and Conjard (for adrenergic fibres) or by Gerebtzoff (for acetylcholine-esterase). French scientists (*e.g.* Tinel), more particularly, have pointed out that the result (stimulating or reducing effect) of ortho- or parasympathetic stimulation of an organ depends on various humoral conditions. Changes in the O_2/CO_2 or K/Ca ratio (see p. 183) of the fluids surrounding the nerve endings in the stimulated organ may alter a stimulating effect of the ortho- or parasympathetic nerves into greatly reduced processes and *vice versa*. However, so far no positive evidence has been found that a primarily adrenergic reaction in a tissue (demonstrated by the Champy-Coujard colour test) could change into a cholinergic one or *vice versa*.

the excitability of skeletal muscles; it inhibits the intestinal wall; it converts glycogen into glucose in the liver and causes a rise in the blood sugar level. This rise may be so great that sugar is excreted in the urine. Adrenaline also causes contraction of the capsule of the spleen and of the wall of the gall-bladder and relaxation of the detrusor or contraction of the sphincter muscle (closing the urethra) of the urinary bladder. According to Cannon *et al.*[473-475], also the coagulation time of the blood is reduced by strong adrenaline secretion, due to indirect stimulation of the liver, and this increases the risk of thrombosis and embolism in the body (see later). Subcutaneous injection of adrenaline usually increases the red cell count, haematocrit value, haemoglobin concentration and the plasma protein concentration. The white cell and platelet count may likewise rise.

Acetylcholine, on the other hand, causes the pupils to contract, certain peripheral blood vessels to dilate and the bloodpressure to drop ($1 \cdot 10^{-5}$ mg is enough to do this); it slows down the heartbeat (concentrations of $1 \cdot 10^{-8}$ mg are sufficient); it stimulates lacrimal secretion and the production of gastric and pancreatic juices and increases movements of the oesophagus, stomach, intestines and bladder; it helps to transmit the nerve impulses to the muscle fibres (muscular contraction) and so forth.

It will be evident that any climatic or meteorological stress condition affecting either the ortho- and parasympathetic nervous system could influence a very large number of physiological processes in the human body and might be pathogenetic if the morbidity limit of an organ (see p. 29) is reached shortly before stimulation impinges upon it. The studies of Hoff [500-502], Braun[466], Lungewitz[520] and Wesseling[558] are interesting within this context. According to these authors, an increase in acidity of the blood serum and urine is noted during periods of pronounced orthosympathetic stimulation, whereas, during typical parasympathetic conditions, these fluids are more alkaline. Hoff states that this acid condition of the blood capillaries is always accompanied by contraction of the blood capillaries of the brain, causing *migraine* and depressive conditions. Similar processes seem to occur during the menstrual cycle and disappear or decrease if alkaline substances (*e.g.* antacids) are given to the patient.

Where *asthma* is concerned it is an interesting fact that the smooth muscle fibres of the bronchi receive dilator fibres from the ortho-sympathetic nervous system and constrictor fibres from the vagus (belonging to the cranial division of the parasympathetic nervous system). Reflex stimulation of the latter system may cause contraction of the bronchi resulting in an attack of asthma, whereas adrenaline secretion causes a relaxation of the muscle wall of the bronchi.

It is well known that *histamine,* like acetylcholine, also induces a fall in blood pressure and causes bronchial spasms due to constriction of the pulmonary arterioles. Histamine is normally present in the blood in small quantities, probably derived from the eosinophil leucocytes. It may, however be liberated in larger quantities, causing bronchial spasms and dyspnoea (see pp. 460 and 464), as a result of injury to the human skin, infections, inhalation or consumption of certain substances.

Physical and emotional stress, also climatic stress (*e.g.* cold) and a sudden drop in arterial blood pressure (*e.g.* due to overstimulation of the parasympathetic nerves) are known initiators of increased adrenaline secretion, enabling the body to deal adequately with the new state of emergency.

In the previous section the various antagonistic processes of both nervous systems have been oversimplified to facilitate the understanding of these very complicated processes. In reality, as in all processes in nature, the physiological processes involved are considerably more complicated and are still very little understood.

(3) The *peripheral nervous system.* Even more complex is this third autonomic nervous system. Its significance and function has always been a point of considerable controversy. Recent histological studies, notably by Meyling[524-525], have demonstrated that this system probably consists of two parts: a peripheral intrinsic network of small autonomic ganglion cells (the *interstitial* cells of Cajal) and a synaptically built reflex system of afferent and pre- and postganglionic ortho- and parasympathetic nerve fibres, the end ramifications of which are connected with the terminal network of autonomic cells in an apparently synaptic way.

The peripheral nervous system in the cutis and epidermis of the skin may act as the receptor of external stimuli (changes in temperature, radiation, electric properties of the atmosphere, etc.). These exteroceptive stimuli are transmitted to the brain centres along the peripheral myelinated nerves of the CNS and along the various afferent paths to those centres. A considerable part of the received exteroceptive stimuli reach the *formatio reticularis* of the brainstem and the nuclei of the hypothalamus, which in turn affect the autonomically and endocrinologically controlled processes in the body.

Recent neuro-anatomical studies suggest that only part of the exteroceptive stimuli (*e.g.* pain stimuli), which reach the CNS along afferent nerve fibres, are transmitted to the cerebral cortex through the thalamus. It has been demonstrated that part of the stimuli reach the cortex without interference of the thalamus opticus.

The peripheral nervous system seems to be also responsible for the tonus of cell fluids and their diffusion (*e.g.* in the artery walls), the interstitial cells acting as tension receptors. In view of these observations it is possible that the peripheral nervous system plays an important role in the causation of arteriosclerosis.

2. *Differences in Biometeorological Reactions*

We stated in the previous section that, whereas adrenaline causes constriction of the arterioles and capillaries of the skin, acetylcholine tends to dilate. The former process occurs immediately as a reaction to a sudden fall in environmental temperature, because the contraction of the capillaries diminishes the loss of heat by the body. A discussion of the detailed mechanisms involved will be given in the following sections on thermoregulation.

The example given clearly indicates a different reaction of the human body in response to different air mass influxes (see p. 17) and passages of fronts. As the adrenaline and acetylcholine reactions are directly controlled by the ortho- and parasympathetic nervous systems, it has always been a point of great interest to bioclimatologists to find a simple test to determine whether specifically the ortho- or parasympathetic nervous system is most involved during sudden changes in the rate of environmental cooling (due to changes in temperature, humidity and air movement, see p. 225). In the following pages we shall briefly review various studies on the difference in reaction of the autonomic nervous systems as a result of changing environmental meteorological conditions.

Studies by G. Straube, A. Kalkbrenner, K. H. Scholz and F. Becker*[463, 545, 546] *around 1950*

Electrophoretic adrenaline and acetylcholine skin tests of the thorax demonstrated in the same person pronounced differences in excitability of the ortho- and parasympathetic nervous systems under different weather conditions. This difference showed up in different size of vesicles on the skin (in the case of adrenaline) or degree of reddish colouring of the skin (in the case of acetylcholine) after application of the electrodes. The actual procedure was for the anode (5–12 cm), after being impregnated with the solution, to be placed on the second dorsal segment of the thorax for 3–5 minutes. Three grades of vesicles or colours** were distinguished. The average values

* Formerly Chief Surgeon of the Provincial Hospital, Hofheim (Taunus, Germany).

** The colour reaction was divided into 3 groups: slightly reddish colour under part of the electrode surface (weak reaction); reddish colour equally distributed under the whole surface of the electrode (medium reaction); marked reddish colouring exceeding the boundaries of the electrode (strong reaction). It proved to be very easy to obtain objective values for these colour estimates.

of 12–15 people tested at the same time were taken as an average value for that particular period. It is realized that the reaction depends on the concentration of the solution, time of application, kind of electrode and current used. However, by keeping all these factors constant, different reactions were observed on certain days. Electrodes were impregnated either with a 1 : 6000 solution of adrenaline or a 1 : 40 acetylcholine solution (previous experiments had demonstrated that both concentrations give comparable results); the electric current was 10 mA; number of patients 49 (living under the same conditions at a health resort), observed for 54 days, giving 607 observations. Experiments were carried out for 6 months, in other words before, during and after the passage of fronts, foehn and other important meteorological weather changes. After the six-month period was over, the clinical data were studied in close cooperation with F. Becker, head of the Meteorological Institute at Königstein (Taunus, Germany), in relation to weather conditions. Therefore, the clinician did not know the exact weather conditions prevailing during the experiment, which minimized the possible influence of this subjective factor. The following results were obtained:

(1) During quiet atmospheric conditions the colour changes of the skin were weak.

(2) They were strongest during the passages of fronts and after sudden changes in air mass. The more abrupt the weather changes, the stronger was the colour reaction. The strongest reactions were observed if a number of fronts passed the station at short intervals before the day of the skin test.

(3) Both cold and warm fronts affect the ortho- and parasympathetic nervous systems, but there usually seems to be less delay in reaction when cold fronts are involved.

(4) The acetylcholine reaction, as a result of change in air mass, always set in earlier than the adrenaline reaction.

(5) The parasympathetic reaction often occurred 5–6 hours before the actual passage of the front and pronounced air mass change. The orthosympathetic (adrenaline) reaction became stronger about 3–5 hours after the passage of the front; in other words, after a strong parasympathetic stimulation had taken place for almost 8 hours.

(6) In a number of patients the increased stimulation could be observed 16–30 hours after the passage of the front.

(7) The observations under (4) and (5) apply to the average values obtained from 49 adult persons. In individual cases, when the person had a particularly unstable sympathetic nervous system, a different reaction was observed. In such cases the adrenaline reaction may start before the acetyl-

choline colouring. A similar phenomenon will be discussed on p. 269. It was found that the effect of environmental conditions on the thyroid is also often different in people with an autonomic nervous system of subnormal stability.

(8) Certain weather conditions, *e.g.* foehn may cause very strong skin reactions in summer and autumn but not in winter.

(9) The higher the altitude of an inversion layer (see p. 19) in the atmosphere, the stronger appears to be its effect upon the human organism.

Studies by F. Becker, W. Catel and E. Klemm*[163]

Similar evidence was found by Catel and Klemm, who submitted children to their experiments. These two authors applied *suprarenin* (instead of adrenaline) to the skin, using *pilocarpine* ($C_{11}H_{16}N_2O_2$) for parasympathetic stimulation. During the experiment the blood pressure and pulse frequency of the children were recorded continuously. The drugs were injected subcutaneously. Either 0.2–0.5 cc suprarenin hydrochloride, 1:1000, or 0.0015–0.0025 g pilocarpine hydrochloride was used, depending on the age of the children. Injections were given before and during passages of fronts. Blood pressure and pulse frequency were recorded every 5 minutes before and after the injection, other clinical symptoms, such as changes in pallor, perspiration, shivering, skin vesicles, etc., also being continuously observed.

Similar experiments were carried out during periods of quiet weather conditions.

A total of 19 children of $3^1/_2$–$16^1/_2$ years of age, including mild cases of inactive, often regressive, tuberculosis, were studied. The following results were obtained:

(1) *Suprarenin test.* In 11 children of $7^1/_2$–$16^1/_2$ years the injection caused the following increases in blood pressure and pulse frequency:

	Blood pressure increase	Pulse frequency increase
During quiet atmospheric conditions	7%	13%
Warm front	17%	27%
Cold front	18%	23%
Foehn	13%	11%

(2) *Pilocarpine test.* In 8 children of $3^1/_2$–$12^1/_2$ years a lowering of these factors was observed.

* Formerly Chief Surgeon of the Pediatric Clinic, Mammolshöhe (Taunus, Germany).

	Blood pressure decrease	Pulse frequency decrease
During quiet atmospheric conditions	3%	8%
Warm front	13%	7%
Cold front	5%	2%
Foehn	10%	3%

(3) In the absence of previous medical injections, the passage of fronts did not change the blood pressure of the patients.

The results obtained by Catel and Klemm suggest the following interesting conclusions: Both cold and warm fronts seem to affect the sympathetic nervous system. In children, however, the orthosympathetic nervous system seems to be relatively more affected than the parasympathetic (which, according to Catel, is usually more highly strained in children than in adults). In the case of pilocarpine tests, only warm fronts and foehn seriously lower the blood pressure. The pulse frequency slows down less during the passages of fronts than during quiet atmospheric conditions. The phenomena described were particularly evident in the middle of the summer during the passage of cold fronts.

In addition to pronounced drop in blood pressure and pulse frequency the suprarenine tests showed larger skin vesicles, increased general unrest and tremor, etc. Pilocarpine caused larger and more persistent dermatographic phenomena in summer than in winter.

The observations by Straube and Catel *et al.* are supported by the observations of Sargent, Nedzel and others described on p. 588. According to these studies, the toxicity or general physiological effect of certain drugs (*e.g.* adrenaline) changes depending on the day of injection with respect to the period of air mass influxes.

Studies by K. Hansen and Michenfelder[497]

Similar fluctuations in skin tests have been observed by Hansen and Michenfelder (at the University Medical Centre of Heidelberg, Germany) in relation to pollen skin tests for hay fever. Desensitizing tests on 105 hay fever patients showed considerable fluctuations. During quiet weather conditions (high barometric pressure) the skin reaction was weak as compared with days of great atmospheric turbulence (low pressure periods). Also a period of strong ultraviolet radiation, preceding the injection, decreases the skin reaction.

The degree of meteorotropic effects, after stimulation of the nervous systems, depends on previous excitation of the nervous system (J. Wilder's law of the initial value[559]*)*

Round about 1930 Wilder introduced an important physiological principle known as the *law of the initial value*. This general biological law states that the result of a stimulus depends on the previous history; in other words, in a physiological process the higher the initial value, the less the tendency is there for the initiated process to increase. As a result, after previous stimulation by large doses of adrenaline, for example, renewed application of adrenaline to the skin will produce only a slight increase in the physiological effects, with a steep fall as soon as the application ceases. If only small doses have been given, renewed applications will have strong biological effects, followed by a gradual diminution. In the latter case the maximum biological effect observed is usually greater than in the previous case.

This law of Wilder's can also be applied to the autonomic nervous system. The higher the previous excitability has been, the smaller is the increase after renewed excitation, the stronger will the counterbalancing reactions be. Put differently during physiological processes in organs where the ortho- and parasympathetic nervous systems have antagonistic effects, after very strong stimulation of one of these systems, even a mild stimulus may cause an antagonistic reaction. Similar phenomena are known from single nerve or muscle stimulation. Cole[478] was able to demonstrate Wilder's law as applying to *electrical excitation of nerves*. His observations can be summarized as follows:

(1) An electric stimulus, however weak or brief in duration, will leave the nerve in an altered state of excitability.

(2) The excitability, after reaching a maximum, tends to return to its resting value, known as *accommodation*.

(3) By increasing gradually the intensity of the electric stimulus, a sudden strong electric stimulus may pass without causing any further stimulation.

Similar phenomena are known in *muscular stimulation*:

(1) Successive stimulation of a muscle causes the height of contraction soon to reach a maximum and then begins to fall off. It becomes *fatigued*.

(2) Stimulation in rapid succession of a muscle, which has not been stimulated before, will rapidly increase the degree of tension of the muscle. However, this summation of stimuli may not occur if the interval between them is too short.

These general rules are obviously of great interest to the student of various meteorotropic diseases *e.g.* bronchial asthma (see p. 469). In view of the rules described above, it is easy to see that meteorological stimuli following each other in quick succession may cause reactions opposite to those we would expect, as clearly demonstrated by K. Wetzler[780]. In other words, if physiological stimuli caused by certain meteorological factors, affecting the parasympathetic nervous system, for example, were to continue for a considerable time, or operate repeatedly at short intervals, the result might be a stimulation of the orthosympathetic system or *vice versa*. This meteorotropic mechanism is described in biometeorological literature as the *compensation principle of F. Hoff*[503]. If the condition of an organ does not permit of such a counter-regulation, meteorotropic pathological effects usually ensue.

The rules described are very important for the understanding of biometeorological phenomena because it means that the effects caused by the passage of a single cold front or by a cold front preceded by a warm front or two or more cold fronts passing an area at very short intervals may be entirely different. This could also explain the observed deviations of the various known statistically significant biometeorological relationships.

Influence of biological rhythms

Another important feature, which makes it difficult to compare the physiological effects caused by the same meteorological factors, is the influence of the normal endogenous *biological rhythms* of the body, such as the 24 hour rhythm of diuresis, with maximum execretion of water, urea and chloride around 2 p.m. and minimum around 2 a.m. (demonstrated by F. Gerritzen and others); the temperature of the body being highest in the evening and lowest in the early hours of the morning. A similar rhythm exists in the degree of excitability of the autonomic nervous system, which is different at different periods of the day.

Most authors agree that during the night parasympathetic stimulation dominates, either because of greater activity of the parasympathetic nervous system or due to a decrease in activity of the orthosympathetic system. This difference in activity may explain why urine during the night and early morning is usually more alkaline than during the day, that asthmatic attacks are more frequent during the night, etc. More convincing evidence for this assumption was collected by Balzer, Jores and others[460]. They were able to demonstrate that the bilirubin secretion (the iron-free pigment which remains after destruction of the red blood cells) shows a pronounced daily rhythm even under constant food conditions. It reaches a maximum between 8 and 12 a.m. and around 18 p.m. and a minimum at roughly 6 a.m. and between 4 and 8 p.m. Similar changes were created artificially by injecting pilocarpine and suprarenin (see p. 197). Pilocarpine injection (similar to parasympathetic stimulation) causes an increase in the bilirubin level, which reaches a maximum after 50 minutes, becoming normal again after 90 minutes. A suprarenin injection (similar to orthosympathetic stimulation) causes a decrease in the bilirubin level after 30 minutes, which still continues after 90 minutes. The very high values of bilirubin observed during the night, particularly after 3 a.m. strongly suggest the dominating influence of parasympathetic stimulation at this time of the day. Further details concerning these biological rhythms will be given on p. 369.

On p. 390 Macfarlane points out that more sweat is produced during the afternoon than in the morning, at the same air temperature. It will be pointed out on p. 216 that sweating is controlled by parasympathetic stimulation.

Stollreither and Ungeheuer[751] were able to show that, at Bad Tölz (Bavaria, Germany), biometeorological effects can only be observed during the period from noon till midnight, at the beginning of foehn weather. This is a very important observation because it indicates that the effect of the penetration of air masses or fronts will be entirely different if it impinges upon a highly stimulated parasympathetic system at night from what it will be during another period of the day when orthosympathetic stimulation dominates.

Influence of individual differences in physiological pattern

Hoff[500-503] demonstrated the influence of individual differences in physiological mechanism, upon the biometeorological effects in different persons.

In those predominantly subject to severe stress conditions of the orthosympathetic nervous system, the acidity of the blood rises, the potassium-calcium ratio shifts towards calcium, and the blood pressure pattern, etc., will be different from what they are in persons with a highly strained parasympathetic nervous system. These observations might account for some of the differences in type and responsiveness observed in different people under the same meteorological conditions.

This brief summary of the differences in biometeorological reactions of the autonomic nervous systems may make it easier to understand the many apparent discrepancies in biometeorological literature. The differences in the results obtained by various research workers are not necessarily due to observational errors but may be caused largely by the different conditions under which the experiments were carried out.

Subsect. B. FUNCTIONING OF HYPOTHALAMUS AND THALAMUS

1. Hypothalamus

The hypothalamus is a very complex region of the brain, connected with and located below the thalamus, which seems to have integrated control of the three autonomic nervous systems and the secretion of the anterior and posterior lobes of the pituitary (according to Rasmussen connected with the hypothalamus by more than 100,000 fibres). This takes place either through a complex network of nerve fibres (in the case of the autonomic nervous system) or by blood-vessels carrying a chemical substance from the hypothalamus to the pituitary.

The nuclei (see below) of the hypothalamus are probably also concerned with the conditioning of emotional patterns which serve the expression of emotional behaviour.

The hypothalamus is likewise the main centre of heat regulation of the human body, as will be further explained in the following section. It therefore plays a leading part in many aspects of mammalian physiology and its great significance both phylogenetically and anthropologically is generally recognized.

As indicated on p. 188 and in Figs. 36–39, the hypothalamus is part of the lower section of the diencephalon and is located more or less between the thalamus and pituitary. It is bordered anteriorly by the lamina terminalis with the anterior commissure above and the optic chiasm below; posteriorly by the interpeduncular fossa (a depression between pons and cerebellum); dorsally by the hypothalamic sulcus, the junction between hypothalamus and thalamus.

More or less within these boundaries are clusters of cells known as *hypothalamic nuclei* (see p. 189) which are abundantly supplied by blood vessels. In man, unlike some lower animals, these nuclei are not clearly defined areas. Exceptions to this rule are the *supra-optic* and *paraventricular nuclei* and the *mammillary body*. The specific functional significance of these various nuclei is only partly known and requires considerably more research. However, for practical purposes the nuclei have been grouped together into a number of morphologic entities. According to the classification of Le Gros Clark (*The Hypothalamus,* Edinburgh, 1938), three main groups of nuclei can be distinguished.

(1) The *anterior nuclei* comprise the paraventricular and supra-optic nuclei (Fig. 37, B and D) and the infundibular nuclei (Fig. 46). They form a tract along the pituitary stalk (see p. 256) into the posterior parts of the hypophysis.

(2) The *middle nuclei,* occupy the middle part of the tuber cinereum (see p. 189) and include the ventromedial (Fig. 37, H), dorsomedial (Fig. 37, G) and lateral (Fig. 37, E) hypothalamic nuclei.

(3) The *posterior nuclei* comprise the mammillary-infundibular nuclei,

the posterior part of the tuber cinereum and the medial and lateral nuclei of the mammillary body (Fig. 37, I and J).

The mutual connections between these groups of nuclei are still obscure, but descending fibres are received from the cerebral cortex and the thalamus. Efferent fibres pass down into the brain stem and probably to the spinal cord.

The *main functions of these groups of nuclei* are the following:

(1) The anterior nuclei* (particularly the supra-optic and paraventricular nuclei) seem to be the principal regulators of the secretion of the anti-diuretic hormone *vasopressin* and the uterus-stimulating hormone *oxytocin* by the posterior lobe of the pituitary (see p. 259). Local heating of this part of the hypothalamus (in cats, dogs and monkeys) causes vasodilatation of the skin, sweating and polypnoea (Ranson, Magoun and others).

(2) The posterior nuclei seem to affect the orthosympathetic nervous system more especially (see p. 189) Stimulation causes secretion of adrenalin, rise in blood pressure and acceleration of the heart, etc. From the ventral part of the covering thalamus effective pathways for *emotional expression* reach this part of the hypothalamus. Stimulation of the frontal lobe of the cerebral cortex may cause a reflex reaction in the hypothalamus. On the other hand, electric stimulation of the posterior nuclei of the hypothalamus creates a typical reaction of fear in animals together with visceral and muscular manifestations. Lesions of this part of the hypothalamus also bring about *lethargy* (prolonged and unnatural sleep or morbid drowsiness) and *hypothermia*. The first phenomenon is caused by a nerve tract running from the mammillary body to the anterior nucleus of the thalamus and from there to the cortex. Stimulation of the mammillary body produces sleep.

(3) Stimulation of the infundibular nuclei together with the ventromedial and dorsomedial nuclei (see p. 202) has a considerable influence on *sexual behaviour* (for further details see p. 260).

(4) The lateral hypothalamic nuclei influence the internal secretion of ACTH which originates from the basophil cells of the anterior lobe of the pituitary (see p. 257).

(5) The group of small cells of the posterior part of the tuber cinereum has a *regulating influence* on basal metabolism, vasomotoric regulation, regulation of heart and blood pressure, etc.

(6) The medial and lateral nuclei of the mammillary body are concerned with the regulation of the *processes of consciousness*.

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* The axons of the neurons of these nuclei pass down the pituitary stalk and branch to form a dense network amongst the cells of the posterior lobe.

(7) The transitional area between diencephalon and mesencephalon (see p. 188) conditions the *rhythm of the vital processes* of the body, for example the sleep-waking mechanism.

As stated above, the hypothalamus is intimately related to the temperature regulation of the body. Destruction of this area causes prolonged hypo or hyperthermia. As many meteorological phenomena are associated with sudden changes in environmental temperature, the hypothalamus must evidently play an important part in meteorotropic phenomena. Prolonged thermal stress under extreme conditions, such as may prevail in extremely warm or cold climates, may seriously affect our thermo-regulation mechanism.

It is known clinically that diseases of the hypothalamus may be responsible for a number of syndromes, such as changes in personality, disturbed temperature regulation, *diabetes insipidus* (a disease characterized by increased urinary output exceeding 10 litres daily, even 40 litres has been recorded), hypersomnia, adrenogenital syndromes (fat deposition and genital hypoplasia), changes in carbohydrate metabolism, etc. It has not yet been definitely established whether similar syndromes could result from protracted spells of climatic stresses.

We have stated more than once that the hypothalamus is undoubtedly influenced, probably indirectly, by the *great sensory systems of the cortex* with their many thalamic connections. Studies in recent years have revealed that other parts of the fore-brain besides the hypothalamus, together with the thalamus, have a controlling influence on the autonomic nervous systems. This is particularly true for the *rhinencephalon,* the portion of the brain concerned with the sense of smell.

As indicated above, the hypothalamus is *richly supplied with small blood arteries.* They arise in Willis's circle (a loop of vessels near the base of the brain). Both arterial supply and drainage seem to be completely independent of those of pituitary gland and stalk. Thanks to its abundant blood supply, even the slightest changes in temperature of peripheral blood arteries, due to environmental changes in temperature, are immediately recorded by the cells of the hypothalamus. The supra-optic and paraventricular nuclei of the anterior nuclei in particular, are pervaded by a very dense capillary network of blood vessels, which register the slightest changes in the physico-chemical state of the blood in their neurons, because the activity of these neurons seems to be regulated primarily by variations in the osmotic pressure of the blood. *E.g.,* in the case of dehydration of the body, the osmotic pressure of the blood in the hypothalamic vessels increases. The neurons of the supra-optic nuclei immediately respond by increasing the production and/or release of anti-diuretic hormone by the pituitary, leading to a rise in the plasma content. On the other hand, the drinking of large quantities of water lowers the osmotic pressure, which inhibits the secretory activity of the supra-optic neurons.

It is not only changes in blood, however, which affect the supra-optic neurons. Various emotional stress conditions (see above) may affect this part of the hypothalamus, although it is doubtful whether they could neutralize the diuretic osmotic effects mentioned.

The physico-chemical sensitivity of the supra-optic area accounts for the fact observed in recent years that it is not only the posterior lobe of the pituitary which is influenced by the hypothalamus (see above), but also the anterior lobe with its many hormone-producing mechanisms. It is assumed that the anterior lobe of the pituitary is stimulated in a neurohumoral way, *i.e.* partly by nerve stimulation, partly by chemical substances in the circulating blood. For example in non-spontaneously ovulating animals the act of copulation seems to stimulate, through the cortex-thalamus, the hypothalamic neurons, which release a nerve impulse followed by a chemical secretion, this in its turn reaching the anterior lobe of the pituitary through the blood and promoting the release of luteinizing hormones (see p. 257). It is therefore evident that lesions or temporary disturbances of the hypothalamus, *e.g.* due to strong meteorological agents affecting the cooling rate of the body, might considerably influence the production of anterior lobe hormones of the pituitary, with all its pathological consequences.

The anatomy and functioning of the hypothalamus has been discussed rather extensively because of its key position in a great number (if not most) of bioclimatological phenomena. The deeper physiological mechanism of these meteorotropic phenomena and related diseases cannot be fully understood unless the functioning of this important centre in the brain is carefully studied.

2. *Thalamus*

The thalamus (also known as "thalamus opticus") has already been briefly mentioned on p. 188. It is an important sub-cortical centre for sensorial information which receives and forwards sensorial impulses both to and from the cerebral cortex, hypothalamus and other parts of the brain. It is located above the hypothalamus and consists of several nuclei of cells which are divided into different main groups (anterior, posterior, medial, lateral and midline nuclei).

The principal functions of the thalamus are the following:

(1) It acts as a *relay station*. For example, in the corpus geniculatum mediale (one of a pair of small rounded nodules in the lower part of the thalamus) the acoustic pathways are interrupted, in the lateral parts of the corpus geniculatum the optical pathways. The nucleus parateniales thalami (of cats and rats) receives stimuli from the rhinencephalon, a portion of the brain concerned with the sense of smell, consisting of the olfactory lobe, the anterior perforated substance, the subcallosal gyrus and the parolfactory area. On p. 302 this important part of the brain will be discussed more in detail. Also the nucleus dorso-mediales thalami has a functional relationship with the rhinencephalon. The nucleus anterior thalami is part of the emotional circuit of Papez.

(2) The thalamus acts as a sub-cortical *centre of integration* of the different sensory stimuli.

(3) It conditions *coenaeshetic consciousness*. It is assumed that certain nuclei, possibly the anterior and medial nuclei, represent the most essential parts of the thalamus as they seem to act as centre for recognition of "crude" sensations, whereas the cerebral cortex is more responsible for finer distinctions of sensorial stimuli. When the connections with the cortex are severed the thalamus is still recording hot and cold, but also movements of considerably amplitude. Emotional accompaniment (pleasure or pain) however is accentuated, whereas in the intact body these emotional expressions are damped down by the activity of the cortico-thalamic fibres.

(4) It is an important *conditioning centre for the mood.*

(5) It is the sub-cortical centre which conditions diffusely *global sensory cognition.*

The thalamus also considerably affects the pattern of electromagnetic oscillations of the brain cells, which can be recorded by an electro-encephalograph.

The *α-oscillations* (vibrations with a frequency of 8–12 vibrations/sec) are usually most prominent when a subject sits or lies down quietly with eyes closed and mind at ease. Mental effort or emotional excitement depresses this vibration and may even cause its complete disappearance. In light sleep α-waves become slower, larger and less irregular and may disappear in deep sleep.

The *β-oscillations* (frequency more than 20 vibrations/sec) are very common and increase in amplitude during psychic activity but may disappear if the cerebral cortex is disturbed.

Berger showed that drugs with a specific stupefying influence on the thalamus (*e.g.* veronal, luminal, etc.) greatly increase the α-waves of the cortex. The more the thalamus is blocked, the greater are the amplitudes (studies by Koopman and Franke[509]).

Koopman and Franke explained the *blocking effect on our consciousness* as follows: We observe objects as a result of differences in light energy, in other words, by the presence of shadows. If the cortex is either too vigorously active in all its parts, as a result of thalamic blocking, or completely inactivated by drugs having a specific stupefying effect on the cortex (*e.g.* ether, chloroform, morphine, etc.), this condition of "consciousness" cannot be fulfilled. During *hypnotic conditions,* which can be created, *e.g.* by overstimulation of the nervus opticus and nervus oculomotorius as the result of a high intensity of light in our environment, Koopman and Franke observed the same encephalographic changes as those produced during the artificial blocking of the thalamus by drugs. Similar *meteoro-hypnotic* conditions may obtain on hot days of glaring sun when the driver of a car has to concentrate on the road for a considerable time. Some of his reflexes may slow down and orthosympathetic stimulation is often inhibited. The effect of sunlight stimulation of the brain will be further discussed on p. 347. Most likely the thalamus plays an important part in these physiological processes.

Subsect. C. THERMOREGULATION

As, during chemical processes in the living organism, part of the energy is released as thermal energy, all living matter is a source of heat energy. Therefore all internal and external factors, affecting the thermal balance of the living organism are bound to have considerable influence on the various important physiological processes characteristic of life.

In the following sections will be shown that practically all the vital endocrinological and other physiological functions of the body are affected by changes in environmental temperature, particularly if these changes occur rather suddenly. It is therefore comprehensible, that a vast amount of literature has appeared in the past 60 years on the influence of changing environmental temperatures on the physiology of man and animals.

It would be impossible, even in a long article to review all the results that have accrued from these studies. The student of biometeorology is referred to the various publications, a selection of which is given in the refs.[561–794]. A recent publication by Hensel *et al.*[672], giving an excellent review of this fascinating problem, deserves special mention.

In this section a selection was made of some of the outstanding problems related to the thermal balance of the human body, a field of study which is often denoted as "thermoregulation". The selected subjects are the following:

1. Heat balance (heat production, heat loss and diffusion of water through the human skin).
2. Temperature measuring devices (calorimetric and thermocouple recordings).
3. Average temperature pattern of the human body.
4. Biological rhythm and body temperature (diurnal variations and menstrual cycle).
5. Environmental and other factors affecting the body temperature (humidity, air movement, clothing, age, personality pattern).
6. Sensation of temperature comfort and discomfort.
7. Location and function of thermoregulation centre.
8. Mechanisms of acclimatization.
9. Biological effect of air conditioning (on land, on sea).
10. Effect of temperature on joints and fluid viscosities.
11. Effect of temperature on adrenal and thyroid activity and on diuresis.
12. Effect of thermal baths on oxygen exchange and general circulation.
13. General effect of temperature on disease.
14. Methods for testing thermoregulation efficiency of the human body.

1. Heat Balance

Poikilothermic and homoiothermic organisms

Living organisms are classified into two large groups on the basis of their thermal behaviour: poikilothermic or cold-blooded organisms (from the Greek "poikilos" = different) and homoiothermic or warm-blooded organisms (from the Greek "homoios" = equal or uniform).

The poikilothermic organisms comprise all animals (except birds and mammals) having a variable body temperature. Their temperature fluctuates rapidly with changing environmental temperature.

The homoiotherms (birds and mammals) are able to keep their body temperature fairly constant within certain limits. It is usually higher than the ambient temperature and they are therefore known as warmblooded animals, in contrast to the cold-blood poikilotherms. Lesions of the hypothalamus which destroy descending pathways change mammals into poikilotherms; the body temperature no longer remains nearly constant.

Although the individual temperatures of homoiotherms are fairly constant, marked differences are observed between different birds or mammals. According to Eisentraut[619] birds have a higher body temperature than mammals. The temperature of the former usually exceeds 40° C. This is due to their very high metabolism. During sudden influxes of cold air, birds will hide or fall asleep, slowing down their metabolism. Similar processes occur during hibernation (see p. 703).

Considerable fluctuations in temperature are observed in the lower mammals as well as in the poikilotherms. The temperture of bats, for example, may fluctuate between 41 and 20° C (during sleep).

The thermal condition of the living body can be compared to a heated room with enough windows to let heat out if the room is too warm, or to prevent it from getting cold by keeping the windows closed. In a similar way the human body of a homoiotherm keeps a thermal balance by the heat production and heat loss. The human body is provided with various mechanisms for maintaining, almost perfect thermal balance. These thermostatic processes are assisted by the structure of the *skin* and the *water content of the body*.

Structure of the skin

The skin serves to protect underlying parts from injury and invasion of foreign organisms; it serves also as a sense organ and is therefore richly supplied with nerves which enable the body to adapt itself rapidly to changes in the environment. From the surface to the centre the skin consists of three main units:

(1) The *upper skin* or *epidermis* composed of two layers: an outer horny layer or *stratum corneum* (the most protective layer, composed of dry cells that swell after wetting) and an internal layer or *stratum Malpighii*, which by cell division, continuously makes new, upwardmoving corneous cells. The deepest cell parts of the layer contain the pigment *melanin* (see p. 339).

(2) The *true skin, cutis* or *corium*, a fibrous elastic layer composed of connective tissue varying from $^1/_2$–3 mm in thickness, well supplied with nerves and bloodvessels and containing the hair roots, the lubricating or sebaceous glands (near hairy parts of the body) and the sweat glands. The latter (about $2^1/_2$ millions in the human body) penetrate into the epidermis as corkscrew channels and are particularly abundant on the palm of the hand and on the sole of the foot. On the soles and palms the corium bears ridges in whorls and loops characteristic for each individual. The upper part of the corium contains a great number of bulged parts, the papillae, which penetrate into the epidermis. Two kinds of papillae are distinguished: vessel-papillae, containing a network of the finest blood capillary vessels, occurring particularly in places of corneous structure (such as nails) which require much blood, and nerve-papillae containing the nerve endings and

cutaneous receptors for touch and temperature change. Of all organs of the body the surface of the hand has probably more nerve connections with the brain than any other part of the body. In fact, as pointed out by Jones[685], one can hardly think without the hand being influenced by the thought. Tendencies of anger, affection, fear, etc., are immediately shown by movements of the hand.

(3) The *sub-dermal* or *sub-cutaneous connective tissue* composed of a layer of cells connected to the muscles and bones which possess large meshes filled with fatty substances. In this layer the larger blood and lymph vessels and nerves are located.

Whereas the human and animal body are surrounded by the skin proper (*integumentum commune*), the cavities in the body are covered by a membrane (*membrana mucosa*). The tissue structure of the membrane is practically the same as the skin. The surface is composed of exfoliated epithelium cells which, together with a fluid secretion, form a viscous substance, the slime or mucus. The mucus membranes are rich in nerve endings and capillary vessels.

The thermostatic processes of the body are assisted by the various skin structures described as follows:

(1) The *peripheral nervous system* (see p. 194) *in the skin* enables us to experience differences in temperature between the body and its environment. Studies by Blix and Donaldson suggest that different centres exist for registration of cold and heat. They are known as *Krause end-bulbs* for cold and the *Ruffini organs* for warmth.

It has been pointed out by Hensel [672], Stöhr, Kantner and others that these thermoreceptors should not be considered as anatomically sharply defined bodies or end-plates. They are networks of nerves in various layers, one above the other. For example, in the cat's tongue the first layer is located 10 μ below the epithelium, a second layer at 30 μ depth.

Hensel, Zotterman and Dodt[665-669, 673] were able to show that these nerve networks of both cold and heat receptors are characterized by continuous electric discharges (action potentials) even at a constant environmental temperature. The discharge of the cold fibres, however, suddenly increases during cold stress and decreases or disappears in the neighbourhood of heat radiation, whereas the heat receptors increase in discharge during heat stress. Hensel summarized the differences between the two groups as follows:

Cold receptors	*Heat receptors*
Stationary discharge at constant temperature between 10° and 41° C.	Between 20° and 47° C.
Frequency maximum between 20° and 34° C.	Maximum between 38° and 43° C.
Stationary maximum frequency 10 per sec.	3.7 per sec.
Regular discharges at constant temperatures.	Irregular discharges at constant temperatures.
Rise in discharge frequency during rapid cooling.	Same during rapid heating.

It has been found that in all homoiothermic and poikilothermic vertebrates similar laws of thermal stimulation seem to prevail.

The skin consists of a complicated network of such "warm" and "cold" points containing the various nerve endings. Both rise in temperature and electric stimulation of the same nerve ending creates the same temperature sensation. It seems that the human skin contains more thermal receptors for cold than for heat. There is also a difference in threshold for these sensations. According to Waterston the topographic distribution of the heat centres in the skin seems to alter continually. Temperature sense is best marked in the nipples, chest, nose, the anterior surface of upper arm and forearm and the surface of the abdomen. It is less marked on face and hands and only slight on the scalp and in the mucous membranes. Therefore we can drink a fluid at temperatures which would be painful to the hand. The acuteness of temperature sense varies considerably with the condition of the skin and previous stimulation of the sense organs (see law of Wilder, p. 199). It is most acute between 27° and 32° C. At this interval the skin can appreciate temperature differences of 0.2° C. At lower or higher temperatures the sense is less delicate.

(2) The fine *network of blood capillaries* in the upper part of the corium causes a slight change in temperature of the circulating blood which reports this change to the hypothalamus (particularly the supra-optic and paraventricular nuclei of the anterior nuclei), which is richly supplied by small blood capillaries (see p. 204). As indicated on p. 204, these slight temperature changes affect the osmotic pressure of the blood, which in turn influence the activity of the neurons of the nuclei. In a subsection below on the location and function of the thermoregulation centre these complicated mechanisms will be discussed in greater detail.

(3) The presence of a *fatty layer* in the skin, being a poor heat conductor, acts as a heat-insulating layer if the blood supply through this layer is reduced by nervous stimulation. Obese people may therefore be more resistent to cold than people of normal build.

(4) The *development of hair* diminishes the loss of heat from the skin. Since the hair follicles are richly supplied with nerve fibres, the hairs also act as organs of sensation.

The water content of the body

The body cells consist largely of water (about 70%)*. A considerable amount of thermal energy is required to increase the warmth of this fluid through 1° C. On the other hand, an appreciable loss of heat is required to lower the temperature by 1° C.

*According to Dupertuis *et al.*[616] there is an inverse relationship between total body fat and total body water (determined by the antipyrine technique).

These general anatomic characteristics of the homoiotherms facilitate the balance of the two opposing processes in the thermal balance of the body, *i.e.* heat production and heat loss.

Heat production

Under resting conditions heat production occurs mainly in the skeletal muscles, where exothermic oxidative and non-oxidative reactions are constantly going on. Muscular activity raises the body temperature 1° or 2° C. Lowering of environmental temperature causes an increase in "tensing" of the muscles, mostly followed by synchronous contractions of muscle fibres, known as *shivering**.

To a less extent heat is produced in the liver, kidney and viscera due to chemical processes in these organs. The liver in particular is a very important heat producing organ, the temperature of the hepatic vein being often the highest in the body.

Increased oxygen consumption usually increases the production of heat. A general rise of 10° C increases the oxidative chemical processes (and therefore the heat production) two to threefold (Van 't Hoff's law).

The normal heat production, also known as *basal metabolic rate* (BMR)**, depends on a number of factors:

Surface area. The BMR is closely related to the surface area and less directly related to height or weight. According to Du Bois's formula, the surface area

$$A = W^{0.425} \cdot H^{0.725} \cdot 71.84$$

in which A = surface area in cm², W = weight in kg, H = height in cm. BMR in adult males is approximately 40 cal, in females 37 cal/h/m² of body

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* With specially devised vibration recorders, Rohracher [738–740] (University of Vienna, Austria) was able in 1950 to register micro-fibrations on all parts of the human body. In healthy persons the frequency of the vibrations is 6–12c/sec, amplitude 1-5 μ (if muscles are completely relaxed). With tensed muscles the amplitude may increase to 50 μ but the frequency remains the same. During sleep the amplitude decreases to about half the size. With increased thyroid activity or fever the frequency increases to 14 c/sec.

After death the vibration continues for about one hour. The same vibration was observed in a great number of other homoiotherms; it seems to be absent in poikilotherms. During hibernation, long periods without vibration alternate with very short periods with vibration; on waking, the vibrations became normal again (6 c/sec). In view of these observations Rohracher believes that there is a relationship between muscle contraction, body temperature and basal vibration of the body.

** Basal metabolic rate or basal metabolism is the energy output per hour or per day of an individual under standard resting conditions, *i.e.* at complete bodily and psychical rest, 12 to 18 hours after a meal and in an equable environmental temperature. BMR is expressed as percentage above or below the theoretical standard for the individual, taking into account his age, height, weight, etc.

surface (A for adults is about 1.8 m²). Expressed in body weight BMR is about 1 cal/kg/h.

Age and sex. The BMR/m² is considerably greater in children than in adults. At the age of two, the BMR for boys is 57.0 cal/h/m² (according to S. Wright); at 8 years 51.8; at 10 years 48.5; at 16 years 45.7; at 20 years 41.4; at 30 years 39.3; at 40 years 38.0; at 50 years 36.7. For females the BMR for these age groups is: 52.2, 47.0, 45.9, 38.8, 36.1, 35.7, 35.7, 34.0. Hence, in the same age group the average BMR is less for females than for males.

Activity of ductless glands. Thyroxine (see p. 268) stimulates the metabolic activity of the body considerably. In exophthalmic goitre (see p. 269) the BMR may increase to double the normal. In myxoedema (see p. 268) BMR may be depressed to 60% of the normal value. As thyroxine production is regulated by the thyrotrophic hormone of the pituitary (see p. 257), any environmental condition affecting the hypothalamus and pituitary influences general metabolism. As stated on p. 257, the pituitary growth hormone also has a direct influence on metabolism.

Adrenaline secretion. This increases the BMR (but less than thyroxine) as a result of increased oxidation in the tissues generally, by constricting the skin vessels (diminishing heat loss) and by stimulating the conversion of liver glycogen into glucose, providing thermal energy.

Temperature. For every rise of 1° F in the internal temperature of the body (for example with fever) the BMR increases by 7%. Exposure to cold below 14° C increases the BMR in order to raise the heat production and to maintain the normal body temperature. This increased BMR is partly due to increased muscular activity, partly to increased secretion of adrenaline and thyroxine (see above). A cold bath may increase metabolism by 80%. Exposure to prolonged heat decreases the BMR.

Food. The taking of food stimulates the BMR, being least with carbohydrates and fats, most pronounced with proteins; starvation or prolonged undernutrition decreases the BMR considerably.

Muscular activity. Violent exercise may increase metabolism over 16 times (oxygen consumption may rise from 250 cc to 4 litres, see p. 293).

Heat loss

A completely insulated human body, without heat loss to or gained from the environment would rise in temperature about 2°C/h as a result of the normal resting BMR. In reality the living organism loses heat like every inanimate body.

As fully described on p. 33 and following pages, the transfer of heat, and therefore the loss of heat, depends on four different physical mechanisms: *conduction, convection, radiation* and *evaporation.* The physical principles involved were discussed extensively on pp. 33–38. Only a few general remarks will be made in the present section.

(1) *Conduction.* The human body has been described by Aschoff[563] and others as consisting of an outer insulating surface layer of varying thickness and temperature (a poikilothermic buffer) and a homoiothermic core. From the heat-producing core a flow of thermal energy passes through the surface layer, partly by conduction and partly by convection currents in the blood stream. This process has been described mathematically by Aschoff and others.

The total heat flow to the skin depends on the conductivity of the superficial tissues (roughly 11 cal/m²/h/°C) and the temperature gradient between core and skin surface, which varies in steepness depending on the conductivity of the inner tissues. Epithelium and fat have a low thermal conductivity of about 0.0005 (cork: 0.0007). The gradient beneath the skin is particularly steep, *viz.,* approximately 8°C/2.2 cm. Blood circulation may reduce this gradient to 1°C/2.2 cm.

A decrease in environmental temperature leads to vasoconstriction and lowering of the skin (surface) temperature. Decreased conduction raises the core temperature. A rise in environmental temperature causes a reversed process. As vasoconstriction is controlled by the orthosympathetic nervous system, in individuals with unbalanced autonomic nervous systems vasoconstriction may be delayed or less effective than in normals and as a result the tissues of the surface layer could be seriously affected by the lowering of temperature. The physiological processes as a result of this lowering of temperature (see later) may cause an imbalance of the thermal regulation centre. Such processes most likely prevail in many rheumatic patients, who are known to have a poor thermoregulation mechanism.

(2) *Convection* (*ca.* 15% of total heat loss) is more responsible for actual heat loss than conduction. Owing to the low specific heat of air (0.24 cal/g), the temperature of the air near the skin rises quickly. With normal convection currents in the air, a thin layer of 1–2 mm of air in contact with the body becomes humid, warmed and lighter. As a result it rises and is replaced by cooler, drier air. At an air temperature of 34.5° C, convection loss falls to zero; above 37° C it becomes negative, *i.e.* the body warms up by convection. Movement of the air increases convection. At medium velocity (up to 30 m/sec) heat loss through convection increases roughly with the square root of air speed.

It was stated on p. 34 that heat loss by convection is a very complicated problem. It depends not only on the $^5/_4$ power of the difference between the temperatures of the object and that of the surrounding air, but also on the shape, size and orientation of the body and the speed of the passing air stream. It was also pointed out that it makes no appreciable difference in the non-evaporative heat loss of a warm body, like the skin, whether humidity of the air be high or low (for further details see p. 35).

(3) *Radiation* of heat from the body surface amounts to about 60% of total heat loss. The human skin, irrespective of its colour, behaves like a perfect "black body" (see p. 37), *i.e.* it radiates strongly at a rate proportional to the fourth power of its absolute temperature (Stephan's law), emitting waves of 5–20 μ wavelength, maximum at 9 μ.

As pointed out on p. 36, with rising temperature of the body the wavelength of the maximum radiation intensity becomes shorter (*i.e.* more energy radiated as shorter electromagnetic waves) and the intensity of this maximum radiation is proportional to the 5th power of the absolute temperature.

The rate of heat exchanges with the environment depends on the difference between the fourth powers of the absolute temperatures of the body and of the environmental objects (see p. 37). Therefore, for a given skin temperature a drop in temperature of a wall, for example, will cause a rapidly increasing heat loss by radiation from the area of the body turned towards this wall. In other words it will depend on the posture of the body.

If a person lies in bed covered by a number of blankets and during the night the room cools off considerably, the smaller heat insulation of the mattress below the body may cause greater loss of radiated heat on the dorsal and lumbar part of the body. This may disturb the regular conduction processes from core to surface layer, as explained above, and causes an excitation of the hypothalamus and the autonomic nervous systems. This process may explain, at least partly, the rheumatic pains experienced during sudden weather changes in the night even if an individual is completely covered by thick blankets. The same probably applies to an asthmatic patient if his thermal regulation is disturbed during sleep by weather changes. In this connection we may refer to p. 82, where the close interrelationship between internal micro-climate of rooms and buildings and external weather conditions was fully described.

(4) *Evaporation* of water from the skin and lungs is another important mechanism by which heat is lost if the internal body becomes overheated. It amounts to about 25% of the total heat loss in a resting person.

Water is lost from the skin by insensible perspiration and sweating.

During *insensible perspiration* this invisible and intangible loss amounts to about 600–800 cc/24 hours, which is about double the water loss at rest from the lungs. The amount lost is about the same over the whole body surface except for the following places, where it is considerably higher: face, neck, dorsum of hand, soles and palms (highest). The process of insensible perspiration consists of the passage of water through the epidermis by diffusion of tissue fluid. The quantity diffused increases slightly with rising environmental temperature and increased blood-flow and falls a little in humid surroundings.

Sweating occurs by two kinds of sweat glands in man. The *eccrine glands,* distributed over the whole body, secrete a dilute water solution containing NaCl (0.1–0.37%, according to Kuno, 0.5–0.9% according to Hill), urea (0.03%), sugar (0.004%) and, during exercise, lactic acid (0.07%). These eccrine glands are densest on the palms and soles, next on the head and least on trunk and extremities. A second group of sweat glands is known as *apocrine glands,* found in the armpit, round the nipples, etc. They secrete a fluid with a characteristic odour.

The functioning of the sweat glands is controlled by cholinergic fibres of the sympathetic nervous system, *i.e.* they are stimulated by acetylcholine, not adrenaline. The actual secretion is produced by direct or reflex stimulation of the centres in the spinal cord, medulla, hypothalamus or cerebral cortex.

Below an environmental temperature of 25° C a resting individual usually does not sweat and evaporative loss, which is proportional to the metabolic rate, is entirely due to "insensible perspiration". Sweating begins slowly around 28° C, but actually begins at an environmental temperature of 29° C (or a body temperature of 35° C). Above 35° C all body heat is lost by evaporation. The heat loss by evaporation is 0.58 cal/g. The rate of evaporation depends on the temperature, the difference between the partial pressure of the water vapour of the wet surface and that of the air immediately adjacent to it, the geometrical surface of the body (see p. 38), the nature and velocity of the airflow, resistance to the flow of water from the interior of the body to the surface (partly depending on the permeability of the membranes and factors affecting this permeability, see p. 335). When the environmental temperature rises slowly from 20 to 40° C, there is a long latent period before sweating begins. It starts quite suddenly and usually all over the skin (except on the palms and soles) and usually coincides with the rise of the internal (rectal) temperature. The sweating may continue to increase even when the room temperature declines.

Sweat secretion is increased by various mechanisms: (a) *Rise of environmental temperature* ("thermal sweating"), *e.g.* by sudden influx of warm tropical air masses in summer, hot baths, high frequency electro-magnetic induction (*e.g.* used in "thermotherapy", see p. 615); (b) *Emotional states* ("mental sweating") when sweating is usually limited to the palms, soles and armpit and is caused by impulses from the higher brain centres; (c) *Exercise* where both mental and thermal sweating are involved.

Sweating can be affected artificially by local application of cold or by drinking cold water (reflexly inhibiting sweating) and by changing the posture (if one turns on to one side the dependent side ceases to sweat and the upper region sweats more). The maximal rate of sweat secretion is usually 1–2 l/h. In extremely hot (shade temperature 34–38° C) and dry regions (humidity less than 30%) the sweat output may be almost 80 litres in 14 days, salt excretion being very high. During thermal acclimatization (see p. 385) the salt content of the sweat decreases considerably.

Response to thermal change

During a period of increased heat production (due to exercise, emotional stress or suddenly raised environmental temperature) the thermal balance is regained by a number of physiological processes:

(1) *Increased blood flow through skin and subcutaneous tissues.* This leads to a rise of skin temperature and therefore to a greater temperature gradient between body surface and environment. Although the heat loss by radiation increases, it is only 15 cal/h for each 1° C rise of skin temperature. Also, heat loss through conduction and convection is insufficient. Therefore the main heat loss is produced by the following mechanisms:

(2) *Increased secretion and evaporation of sweat.* Heat loss by radiation and convection is only possible as long as the external temperature is lower than that of the body surface. If the external temperature is higher than that of the body heat loss results only from evaporation of sweat.

(3) *Vasodilatation of the arterioles of the skin* due to parasympathetic stimulation.

(4) *Increased pulmonary ventilation* (see p. 292). It leads to alkalaemia of the serum and secretion of more alkaline urine. A similar alkalaemia may be produced by a sudden cold stress, increasing general metabolism, oxygen requirement and pulmonary ventilation.

During short exposure (of several hours) to great heat, the *plasma volume* is maintained because the raised osmotic pressure of the plasma proteins attracts fluid from the tissue spaces (see blood volume, p. 322).

Diffusion of water through the human skin

It was pointed out that the skin serves to protect underlying parts and one may be inclined to think that no fluids can penetrate through the skin into the deeper parts of the body. In other words, the transfer of water in the human skin seems to be unidirectional and restricted only to the two processes, described above, sweating and insensible perspiration. However, experiments by Buettner[169-171] and Folk and Peary have demonstrated that this assumption is not correct.

(1) A closed box containing 100 cc of water, in which a human foot or arm is exposed to water, will indicate a loss of water of 2 cc/h. A small portion is apparently absorbed by the stratum corneum of the skin, the major portion entering the system, which could be demonstrated by using radioactive isotopes, *e.g.* heavy water. The fluids entered the blood and were excreted later by the urine. This water transfer has been observed for periods exceeding 50 hours.

(2) Not only water, but also water vapour penetrates the skin in a similar way to water.

(3) The water or vapour intake increases when a person is warm or active.

(4) The same experiment with salt water with concentrations exceeding 5% NaCl shows a decreased water uptake with increased salinity; with 10–15% NaCl solution the transfer ceases. Stronger solutions draw water out of the skin.

(5) Similar water absorption is observed in plants in arid regions. They are able to absorb water vapour from the air or dew deposited on the leaves during the night.

This capacity of the skin to absorb water vapour may explain the sensation of penetrating cold if the human body is exposed to cold and very humid environments. As stated on p. 35, there is no appreciable difference in the non-evaporative heat loss of a warm body, like the skin, whether humidity of the environment is high or low. This seems to contradict the general experience that cold humid air is very unpleasant. However, as pointed out by Burton[598], the absorption of water vapour in the skin probably increases the thermal conductivity of the skin near the receptors. This problem will be further discussed on p. 225.

2. *Temperature Measuring Devices*

The earliest thermoregulation studies of the human body were carried out in large *calorimeters*, for which purpose a bath of water was used in which the human body was immersed. This method was fully described in 1875 by C. Liebermeister (*Handbuch der Pathologie und Therapie des Fiebers*, Leipzig, 1875). His method was improved by J. Lefèvre in 1911 (*Chaleur animale*, Paris, 1911). In later years air chambers were often used, but for the study of small body parts Burton and Bazett[596] still recommend a water bath as a very useful calorimeter, because the heat exchange between body and environment is more efficient in stirred water than in air. Another advantage is that the immediate surface temperature of the body is very close to the water temperature. It was found that changes in bath temperature from 30.28 to 35.52° C cause a rise in rectal temperature of 5.24° C after 10 minutes; a rise from 33.0–33.57°C in the bath is recorded as a rise in rectal temperature of 0.57° C after 25 minutes.

In recent years Dubois and Hardy, Benedict, Bothe and others developed well insulated air calorimeters to study more accurately the mechanisms involved in heat loss and the maintenance of internal body temperature. For this purpose a heat-insulated large box has to be constructed, valididating the law of the conservation of energy for the human body and its immediate environment.

In most of the older calorimeters the response time was far slower than the rate of heat transfer from the subject to the measuring system, which limited the measurement of the total heat output. These various problems were satisfactorily solved by Benzinger and Kitzinger[586] at the Naval Medical Research Institute at Bethesda (U.S.A.). A rapidly responding calorimeter for the continuous recording of biological heat exchange was developed in 1948. The human body is enclosed in a shell completely lined with a uniform heat flow metering layer. This layer, also known as "gradient layer", consists of ribbons of constantan and copper which are interlaced in such a manner through a layer of squares of a transparent plastic that all copper-to-constantan junctions are located above and all constantan-to-copper junctions below the plastic sheet. Plastic and metal are firmly bonded by adhesive foil. This gradient calorimeter has a very rapid response to heat changes of the body, with a time lag of only 42 seconds. The various thermal factors, such as radiation, conduction, convection and evaporation from the skin, and respiratory losses of calories reflected either in temperature or humidity of expired air, are recorded as one single thermoelectric potential. For further details see ref.[586].

Another approach to the problem of body temperature recording is the application of *thermocouple devices* for skin and body temperature measurements. An extensive review of the factors affecting skin temperature and the various measuring devices up to 1938 was given by Murlin[719]. A more recent review up to 1950 was compiled by Stoll and Hardy[648]. In all these devices rapidity and accuracy of measurements are essential. Both thermal conductivity and radiation measurements are required for the study of the heat balance of the body.

For the conductivity measurements very small skin contact instruments are used, known as *thermocouples*. The thermocouple junctions, which are applied to the skin, consist often of enamelled copper and constantan wires, bound with silk thread and silver-soldered together at the tip. A change in temperature of the metal junction creates a thermo-electric potential of a few mV which is recorded by a very sensitive galvanometer which is able to register changes in temperature of 0.1° C or less. Various errors may arise during temperature recordings, such as errors in calibration of the measuring instrument, the effect of the applicator itself in changing the skin temperature (because of difference in temperature of applicator and skin), the influence of pressure of the applicator (causing vascular changes as a result of skin deformation), etc.

Whereas the larger research centres of the Naval, Land and Air Forces in different countries usually use specially constructed automatic skin temperature recorders for individual research, various smaller instruments can be used, *e.g.* the Leeds and Northrup 6-lead Temperature Recorder (U.S.A.), the recorder of Hartmann & Braun (Frankfurt, Germany), the Cambridge Instruments (London, Great Britain) or the Elektrolaboratoriet Electric Universal Thermometer (Copenhagen, Denmark). This latter type of instrument with a carefully balanced sensitive galvanometer has a special construction for automatic compensation of any variation in room temperature and is therefore always ready for immediate use.

All these instruments have plug-sockets by which six or more applicators can be connected (usually by means of a connection box). These various thermocouples can be applied to different parts of the body and give an almost instantaneous reading of skin temperatures at 6 or more places of the body.

The temperature range of these instruments is usually between 0° and 50° C. Often different types of applicators are used, depending on the purpose of the study: instant or stationary measuring of the skin temperature, rectal temperature (body temperature) measurement, etc.

In addition to these thermal conductivity measurements, direct heat radiation measurements should be carried out, for which purpose the Stoll-Hardy Radiometer (produced by Williamson Development Co., U.S.A.) or the Large Surface Thermopile with portable galvanometer (produced by P. J. Kipp, Delft, The Netherlands), for example, have proved to be extremely useful. In the Stoll-Hardy Radiometer the radiant heat energy is detected by rapid-response thermistors which are able to record temperature variations of 0.1° C.

3. Average Temperature Pattern of the Human Body

As the skin temperature of the same human body may vary considerably during the day and in view of the differences between different persons in heat production and heat loss, it may seem rather strange to speak of an average temperature pattern of the human body.

In 1951, at the University of Frankfurt, Lotz and Wezler[702] studied the temperature pattern of four medical students dressed in bathing suits. The students were three young men (20–29 years old, weight 62–67 kg, height 170–176 cm) and one girl (weight 73 kg, height 169 cm).

At normal room temperatures the average skin temperatures were as follows: epigastrium (abdominal surface overlying the stomach) 33.6° C, forehead 33.1° C, breast 32.8° C, forearm 32.6° C, thigh 32.3° C, dorsal part of hand 32.0° C, leg 31.9° C, instep 31.8° C, upper arm 31.5° C. It is evident that these are only average temperatures which will be different for different people. The general pattern, however, is usually the same for all.

Bedford[577] studied the average change in skin temperature in the United Kingdom in relation to air temperature, based on about 1500 persons. He found that on the average a rise of 1° F in the air temperature is accompanied by a rise in temperature of the forehead of 0.14° F, of 0.46° F in that of the hand, and 0.8° F in that of the foot, whereas the average skin temperatures (at an air temperature of 65° F) amounted to 93.7° (forehead), 84.8° (hand) and 76.4° (foot). Hence, with rising environmental temperature the rise in skin temperature is greater on the cooler parts of the body.

The skin temperature of the axilla (armpit) is usually less than 36° C, contrary to the general experience with a normal mercury thermometer kept for 10 minutes in the armpit. Only if the thermocouple (applicator) is kept in the armpit for a considerable time will temperatures exceeding 36° C be recorded because the skin folds will gradually take the internal body temperature which is different from the actual skin temperature of the axilla (being less than 36° C).

4. Biological Rhythm and Body Temperature

The body temperature varies continually, owing to changing internal conditions (general metabolism, muscular activity, etc.) and changes in the meteorological environment. However, in addition to these rather irregular changes, two rhythmic changes have been observed, one of which occurs both in males and females, one in females only.

Diurnal variations in body temperature

As far back as 1839 J. Davy (*Researches, Physiological and Anatomical*

London) reported a daily variation in body temperature based on oral temperature measurements. His observations were extended by W. Ogle (in 1866), S. Ringer and A. P. Stuart (in 1869), T. C. Allbutt (in 1872) and others. However, differences in food, activities, etc. made it difficult to draw any definite conclusions. In 1950 Horvath *et al.*[1180a] studied 11 male and 11 female healthy medical students in Philadelphia. A standard meal was arranged for the entire series. Continuous rectal temperature recordings were made by means of copper-constantan thermocouples and an automatic recording potentiometer. The following results were obtained:

(1) Almost all maximum and minimum temperatures occur between 6 p.m. and 6 a.m.

(2) The first maximum in males occurs around 3 p.m., the second maximum around 8.50 p.m., for females at 10.50 p.m.; the difference in maximum temperatures between males and females is negligible.

(3) The minimum for males occurred around 6 a.m., for females at 4.50 a.m.; the difference between average maximum and minimum temperatures is about 1.5° C.

(4) The mean rate of temperature fall from evening to morning was 0.12°C/h in males and 0.06°C/h in females.

(5) The menstrual cycle had little effect on the general diurnal pattern of the females; only the general temperature level changes (see below).

Considerable variations in the exact time of maximum and minimum temperatures would probably be found if a larger group of people had been studied. The psychological pattern of the person (see p. 201) plays an important role. It would seem that the hour of maximum evening temperature occurs earlier in those who retire and rise early than in the late starters but this matter has not received detailed study yet.

Studies by Horvath *et al.*[1180a] suggest that the diurnal variations are not entirely due to different activities during day time and at night. In order to demonstrate this, 10 healthy males were asked to walk each day for 20 minutes on a motor-driven treadmill at a speed of 4.5 miles/h at about 11 a.m. and 11 p.m. The occurrence of "peak" values of heart rate and body temperature at different times from subject to subject (despite similar working schedules) suggests a diurnal control beyond that of the activity and food cycle only. It has been observed that during sleep there is a diminished control of temperature regulation, which shows itself in dilatation of skin vessels. The diurnal rhythm described changes if the ordinary daily routine is altered, as in night workers for example. After a few days the maxima and minima appear at hours different from those indicated above.

Menstrual cycle and body temperature

In young healthy women the rectal temperature measured immediately after waking up in the morning will be relatively high during the week or 10 days preceding menstruation. Two or three days before menstruation the temperature drops (*e.g.* from 37.0 to 36.4) and remains low till about 10 days after menstruation. It then suddenly rises rather steeply and remains high till two or three days before the new menstrual cycle begins. It has been found that one or two days before the sudden rise in temperature (in between the menstrual cycles) ovulation occurs characterized by the rupture of the follicle and discharge of the ovum, a process controlled by the follicle-stimulating and luteinizing hormones of the anterior lobe of the pituitary (see p. 257). It is this period, immediately preceding the rise in temperature, which represents the period of greatest fertility. A week before or after this rise in temperature a woman is usually sterile. If pregnancy occurs after this rise, no fall in temperature is observed at the end of 10 days and the temperature remains high for several months.

Considering the influence of environmental meteorological conditions on the pituitary (see p. 259), it is not surprising that a sudden change in climate from cold to warm or *vice versa* may affect this menstrual rhythm and the temperature pattern.

5. *Environmental and Other Factors Affecting the Body Temperature*

It is evident that all factors affecting heat production and heat loss may change the body temperature considerably. In this section only the influence of humidity, air movement, clothing, age and personality pattern will be briefly discussed.

Influence of humidity

As stated on p. 35, there is no appreciable difference in the non-evaporative heatloss of the skin in still air, whether the humidity of the air be high or low. Yet everybody knows from personal experience that an increase in humidity during either warm or cold weather may create a feeling of great discomfort. This apparent discrepancy was also demonstrated in the experiments of Burton, Snyder and Leach[598] in 1955. Nine subjects were lying unclothed for 100 minutes at 48° and 58°F with 30% and 80% humidity respectively. Rectal and skin temperatures were measured with thermocouples every minute and the O_2 consumption was measured every 20 minutes. The following results were obtained:

(1) The skin temperatures were practically the same with high and

low humidity. The difference was less than 0.3°C, except for the thorax.

(2) On exposure to cold the rectal temperature rose more when the humidity was low, suggesting a greater physiological response to vasoconstriction. Shivering was greater in incidence and severity when humidity was low.

(3) Sensation of cold was greater with low humidity although the skin temperatures were the same.

Different results were obtained in 1934 by Phelps and Vold[727]. Measurements were made on three female subjects in routine office activity, 3 measurements each time: one on each cheek and one on the forehead. The measurements were done at the same time of the day: beginning, middle and end of each morning and afternoon. They covered the following periods: 1st period 24th March–2nd May 1933 (windows were usually closed, office was steam-heated) and a 2nd period 3rd May–10th June (windows usually open, little or no heating). Wet and dry bulb temperatures and katathermometer readings were taken. The following results were obtained:

(1) A positive correlation was found between skin temperature and room humidity during the closed window season, which was explained as being due to evaporation from the respiratory tract.

(2) A positive correlation with air temperature was observed, *i.e.* a rise in skin temperature of the face of 0.27°C per degree centigrade in rise of room temperature and a 3% shift of total heat loss from radiation and convection to evaporation.

(3) "Comfort votes" of the secretaries were largely determined by their skin temperatures.

These various apparent discrepancies in the reported effect of humidity on human comfort can be explained as follows: It is known that air humidity as such cannot be discerned by the human body; only differences in humidity at a certain temperature are perceived.

Influence of humidity during warm weather. As indicated on p. 216, it is particularly above an environmental temperature of 25°C that a resting individual starts sweating. During muscular activity it begins earlier. Owing to evaporation of sweat on the skin, the body is able to cool off. However, increase in humidity of the environment will reduce the evaporative heat loss*. Therefore high water vapour pressures at high environ-

* At an average skin temperature of 25° C and 10° C environmental temperature, the saturated water vapour pressure of the skin is 23.8 mm Hg. In dry air it would be 0, so the driving force is 23.8 mm Hg. In air saturated with water vapour the pressure gradient would be reduced to 14.6 mm Hg. A reduction in evaporation of 38% would reduce the total heat loss of the body by 25% of 38 = 10% (see above, p. 215).

mental temperatures are experienced as discomfort because they lessen dissipation of heat by evaporation, thus allowing superficial and deep tissues to be warmer than in dry air of the same temperatures. As will be explained in the next section, air movement increases evaporation and is therefore as important as humidity.

Influence of humidity during cold weather. Various factors are probably responsible for the discomfort experienced during cold humid weather: (*i*) As explained on p. 218, the *capacity of the skin to absorb water vapour* seems to be responsible for the increase in thermal conductivity of the skin near the thermal receptors. (*ii*) Behmann[580-583] was able to show that *dry clothes become slightly humid* after short periods of perspiration and, as a result of capillary action, the humidity may reach the surface. The evaporation has a cooling effect on the body, which increases with increasing air movements in the environment. Two kinds of clothing material with equal heat conductivity in dry condition may exhibit great differences in heat loss due to differences in fibre structure and capillary humidity, which becomes most pronounced with increasing wind velocity. (*iii*) *Increased humidity of the walls of buildings,* particularly after rain, causes a strong cooling effect on the wall, especially if the rain is acccompanied by great air turbulence. As explained on p. 36, despite a high room temperature, people sitting near such a wall feel uncomfortable on account of great loss of radiated heat. The same applies to our clothes if we walk about in almost saturated humid air.

Influence of air movement

It is a common experience that as a rule air movement has a cooling effect on the human body. Bedford[577] gave the following clear demonstration of this observation. The skin temperature of the forehead of a subject, wearing normal indoor clothing, was measured at a room temperature of 72°F. It was about 94°F in still air. Afterwards an electric fan was switched on and an air current of 350 ft./min passed over the forehead. After 7 minutes the fan was stopped. The forehead temperature had dropped to 89°F. After the fan was shut off the skin temperature rose, but the rate of recovery was distinctly slower than that of the initial fall. This experiment and the characteristic temperature curve obtained can be used as a simple thermoregulation test (see later p. 251).

If the outside air is still, heat loss declines, because the body is then surrounded by a fairly constant layer of warmed air. Air movement also has little effect on evaporation and cooling, when sweating rate and skin humidity are very low. However, as soon as unevaporated sweat remains on the skin, as a result of higher skin humidities, air movement increases evaporation considerably. At very high temperatures (45–50° C) air movement deteriorates the general condition because convective heat gains over increased evaporative loss.

On p. 43 various mathematical relationships between temperature, humidity and wind velocity were discussed. On an empirical basis many studies were carried out, the most important of which are given in the refs.[561–794].

Lotz and Wezler[702], who studied four medical students (see above p. 221), summarized in Tables 26–28 the changes in temperature of various parts of the skin with increasing wind velocity and at different room temperatures, the relative humidity in these experiments being 50%. Although these figures will not be the same for different people the data give an approximate impression of the rate of cooling or heating of the skin at different air veloci-

TABLE 26

CHANGE OF AVERAGE SKIN TEMPERATURE WITH INCREASING WIND SPEED (DEVIATION FROM ORIGINAL SKIN TEMPERATURE OF 32.5° C)

Air temperature °C	*Changes in skin temperature at windspeed, cm/sec*			
	20	*106*	*203*	*282*
35	+ 1.83	+ 1.84	+ 1.80	+ 1.98
30	+ 0.43	— 0.14	— 1.29	— 0.51
25	— 0.68	— 2.20	— 3.78	— 3.53
22	— 1.85	— 4.35	— 5.29	— 6.48
15	— 3.37	— 7.73	— 10.03	— 11.30

TABLE 27

ORIGINAL SKIN TEMPERATURE OF VARIOUS PARTS OF THE BODY AND SKIN TEMPERATURE AT AIR TEMPERATURE OF 15°C AND WIND SPEED 282 CM/SEC

Original skin temperature °C		*Skin temperature at air temperature 15°C and wind speed 282 cm/sec °C*	
Forehead	33.1	Forehead	21.5
Upper arm	31.5	Upper arm	20.5
Fore arm	32.6	Fore arm	20.8
Dorsal part of hand	32.0	Dorsal part of hand	17.1
Breast	32.8	Breast	24.4
Epigastrium	33.6	Epigastrium	21.4
Thigh	32.3	Thigh	20.7
Leg	31.9	Leg	21.1
Instep	31.8	Instep	15.4

TABLE 28

CHANGES IN SKIN TEMPERATURE OF VARIOUS PARTS OF THE BODY WITH INCREASING WIND SPEED AND AT DIFFERENT ROOM TEMPERATURES (ACCORDING TO E. LOTZ AND K. WEZLER)

Part of body	*Original skin temperature °C*	*Change in skin temperature at wind speed, cm/sec*				*Room temperature °C*
		20	*106*	*203*	*282*	
Forehead	33.1	+2.40	+2.09	+1.99	+1.91	35
		+1.17	+0.32	−1.17	−0.44	30
		+0.52	−1.85	−3.62	−3.18	25
		−0.30	−4.27	−4.94	−6.46	22
		−2.38	−7.92	−10.63	−11.15	15
Upperarm	31.5	+2.75	+3.26	+3.39	+3.40	35
		+0.83	+0.59	−0.41	+0.22	30
		+0.02	−1.19	−2.85	−2.75	25
		−1.68	−3.59	−4.71	−5.67	22
		−3.04	−7.09	−9.16	−10.76	15
Forearm	32.6	+2.11	+2.21	+2.34	+2.35	35
		+0.11	−0.23	−1.23	−0.34	30
		−0.46	−1.56	−3.88	−3.29	25
		−2.00	−3.98	−5.85	−6.72	22
		−2.86	−7.10	−10.00	−11.58	15
Dorsal part of hand	32.0	+2.51	+2.92	+2.77	+2.74	35
		+0.72	−0.44	−1.62	−0.71	30
		−0.68	−4.04	−5.67	−5.56	25
		−3.19	−5.47	−7.23	−8.37	22
		−5.42	−10.63	−13.17	−14.83	15
Breast	32.8	+1.51	+1.76	+1.89	+1.81	35
		+0.31	−0.30	−1.38	−0.41	30
		−0.22	−2.49	−3.07	−3.12	25
		−1.53	−4.16	−4.45	−5.55	22
		−3.11	−7.19	−7.83	−8.55	15
Epigastrium	33.6	+1.39	+1.22	+1.00	+1.11	35
		+0.08	−0.54	−1.77	−1.00	30
		−0.55	−2.29	−3.93	−3.89	25
		−1.62	−4.41	−5.57	−7.11	22
		−3.46	−8.24	−10.42	−11.82	15
Thigh	32.3	+1.36	+1.26	+1.60	+1.73	35
		−0.12	−0.26	−1.23	−0.24	30
		−0.41	−1.68	−3.60	−3.31	25
		−2.33	−4.32	−5.26	−6.20	22
		−3.80	−7.37	−9.98	−11.30	15
Leg	32.0	+1.73	+1.81	+2.01	+2.38	35
		+0.13	+0.06	−0.90	+0.10	30
		−0.81	−1.76	−3.27	−3.11	25
		−2.16	−4.02	−4.65	−6.04	22
		−3.50	−6.40	−8.46	−10.53	15
Instep	31.8	+1.68	+2.33	+2.34	+2.60	35
		−0.74	−1.13	−1.40	−0.86	30
		−1.94	−4.50	−6.28	−5.92	25
		−3.01	−6.07	−7.66	−8.76	22
		−4.72	−10.41	−13.83	−16.47	15

ties. The studies by Lotz and Wezler suggested the following rules, at least in the persons tested:

(1) Air movement accentuates the observed differences in temperatures between different parts of the body, at least below environmental temperatures of 30°C.

(2) A locality with highest temperature in still air does not necessarily remain the warmest spot during air movement. As indicated in Table 27, the succession epigastrium, forehead, breast at still air, for example is reversed with air velocities of 3 m/sec.

(3) At 35°C the skin temperature does not fall but rises at all wind velocities. At 30°C it usually rises as long as the wind velocity is approximately 20 cm/sec. In other words, the effect of air movement is difficult to predict because of an extremely complicated thermoregulation mechanism.

(4) Between 25° and 15°C the skin temperature of the woman used in the experiment dropped more rapidly with increasing wind velocity than that of the males. On the other hand, no shivering was observed in the woman, but was common in the males.

It should be borne in mind that these results do not necessarily apply to other people tested under the same conditions, but it indicates sufficiently the variety of temperature patterns to be expected during air movement.

Another interesting study on the effect of wind chill in Northern Canada was published by Thomas and Boyd[779] in 1957. Instead of the formula used by Bedford *et al.* (see p. 43), they applied the formula adopted by the Quartermaster Corps of the U.S. Army, which was developed by Court[603] in 1948, using Siple's original empirical formula[710]:

$$h = \Delta t \cdot (9.0 + 10.9\sqrt{v} - v)$$

in which h = wind chill or heat loss, v = wind velocity, and Δt = difference in temperature between object and environment. With this formula G.C. Bristow constructed wind chill maps of the U.S.A. Similar maps were made for Canada by Thomas and Boyd, using Siple's formula. Such maps with lines of equal wind chill (expressed in kcal/m²/h) may prove to be of great value for regional bioclimatological studies in those countries.

Influence of clothing

The influence of clothing was briefly discussed on p. 37. This very complex problem will be more fully discussed by Dr. Renbourn on p. 426. Clothing affects the thermoregulation processes profoundly, as it influences the effect of environmental temperature, humidity, air movement and radiation on the human body. This influence of clothing depends on the model, thickness and colour of clothing, the composition and structure of the fibres, etc. As usually 20–30 l of air are present between the clothes, this heat-insulating effect must also be taken into consideration. For further details we may refer to this later section by Renbourn.

Influence of age

Considerable differences in temperature pattern and thermoregulation capacity have been found in relation to age. In *infants* the temperature is first irregular but, with the development of more regular periods of rest and activity, the diurnal variations likewise become more regular. Heat regulation in young children is poor; screaming causes a rise in temperature; a cold bath may lower the temperature by 7° F. In the *aged* the temperatures are low, the body being less active and the circulation being feeble. Their adaptive capacity having become laggard and inadequate they suffer from extreme temperature changes.

The effects of age on finger temperature responses to local cooling in water of 10°C was demonstrated by Spurr *et al.*[752] in 1955. Individuals varied in age from 6 to 83 years. The *Hunting reaction** tended to occur less frequently with the advancing age of the subjects. The rates of cooling and re-warming of the finger suggested a relationship with age which seems to be due to changes in vascular reactivity and (or) a shift in the dominating reactions of the autonomic nervous system affecting contraction and dilatation of the peripheral blood vessels.

Influence of personality pattern

Various studies, *e.g.* by Baker and Taylor[565], Eysenck[621], Henschel[661] and Theron[765] suggest a complex relationship between the psychological or personality pattern of a subject and the type and degree of physiological response to stress-provoking stimuli, *e.g.* cooling of an immersed finger.

Studies by Fine and Gaydos[622] in 1958 on 70 enlisted men of the U.S. Army, who were previously subjected to Psychological Personality Inventory Tests to determine their individual differences, indicated a number of interesting thermal differences:

(1) During cold exposure (*i.e.* subjects, stripped to their shorts, lying in wheel chairs for 30 minutes in a climatic chamber of 70° F, 50% humidity and no wind, were brought to a room of 50° F, 50% humidity and 5 miles/h

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* T. Lewis[699a] described for the first time the phenomenon that if a finger is immersed in water below 15° C, after an initial drop in temperature, sudden rises of 1 or more °C may occur in 5–10 minutes, indicating periods of vasodilatation. These responses are known as *Hunting reaction*. This observation was confirmed and extended by Burton and Eddholm[597, p. 131] and others.

wind velocity) no significant differences in rectal temperatures were found between the different psychological groups.

(2) However, if the personality pattern deviated widely from the norm, the rise in rectal temperature, after the cold exposure had stopped, took much longer than in normal subjects.

(3) No differences were found between these groups in their subjective feelings of cold intensity.

(4) The influence of *body build* was demonstrated by the fact that heavy, big men felt warmer during cold stress than light-weight, small men; the rate of cooling is about the same in these two types. Small men, however, showed faster recovery rates than big heavy men; in a period of continued intermittent cold exposure (*e.g.* during winter) small men suffer less cumulative effect of cold stress than big men.

Preliminary studies of the curves of the "Hunting reaction" observed in various people of the same age suggest considerable differences in relation to their psychological pattern and predominating autonomic functions (see p. 673). However, considerably more work will have to be done in this complex field to increase our knowledge of the relationship between psychological pattern and thermoregulation phenomena. Such knowledge has a clinical bearing, because we may find that, because of their inadequate thermoregulative capacity, subjects with certain psychological patterns are more apt to suffer from certain diseases, such as rheumatism, asthma, etc., than people with a more normal pattern.

6. *Sensation of Temperature Comfort and Discomfort*

Bedford[577] has given an excellent review of the problems encountered in connection with the comfort concept. As our feelings of warmth and cold depend on a number of factors *apart from environmental temperature* (such as air velocity, humidity, clothing, muscular activity, nutrition, age, general body build, degree of acclimatization, rate of perspiration, etc.), different people will experience different degrees of comfort in the same surroundings, some feeling too warm while others complain of cold.

On p. 40 various biometeorological temperature indices were suggested for the determination of the degree of comfort in an average group of normal people. Thom's Discomfort Index (see p. 41) has proved to be particularly useful in summer, at any rate in the U.S.A. Considering the influence of *acclimatization,* the same comfort index usually cannot be applied to different areas. In the U.S.A. with a tendency to over-heating, or the United

Kingdom with a tendency to under-heating, people who are acclimatized to one of these conditions would feel uncomfortable if suddenly transferred to the other area. Generally speaking in W. Europe 65° F is considered to be a comfortable air temperature in rooms.

Another example of the influence of acclimatization on human comfort is furnished by the fact that temperatures which would be found *uncomfortably warm in winter* are experienced as being *pleasant in summer*, because we become acclimatized to higher temperatures in summer. On passing from a warm room into the open air in winter, we usually don extra clothing and are not chilled; but in summer considerable chilling effects are usually experienced on coming from the warm open air into a cold building, the clothing being damp with sweat.

As pointed out on p. 36, it is not only the air temperature but also the wall temperatures of rooms and, therefore, *differences in radiation* between the human body and the walls or floor which are extremely important in our evaluation of comfort.

It is known that women as a rule like higher temperatures than men, which has been interpreted as indicative of a different comfort index. However, experiments by Yaglou and Messer in 1941, during which women were dressed in men's clothes and men in women's, have shown that the difference in sensation of temperature comfort as between men and women is *almost entirely due to differences in clothing.*

Another interesting comfort phenomenon is that a room, despite a sufficiently high temperature, may feel either *stuffy or invigorating.* Studies by Bedford[577], Vernon[774] and others indicated that cool air is more bracing than warm air but the main cause of oppressive feeling is lack of air movement. Adequate air movement (without local draughts) creates an invigorating env ronment. In Great Britain the air velocity should be more than 20 ft./min. It is also found that these air movements should be variable and not uniform, *i.e.* monotonous. In mechanical ventilations the inlets should be so designed that suitable turbulent air movements are created. The physiological cause of this effect of small air movements is partly due to slight evaporation of humidity on the skin but it is also the result of an air exchange. As explained on p. 84, with wind velocities outside buildings of 6–7 m/sec, the air of a room is completely replaced by fresh air as a rule in about one hour due to *wall breathing*; the smaller the rooms, the greater the air exchange (see p. 85). An occupied room will become richer in CO_2 and H_2O and poorer in oxygen (see p. 291). Also, organic substances are given off from the body and clothing and may create a sensation of discomfort owing to the odour which stimulates the rhinencephalon. The ionic content changes and may create a sensation of discomfort, as explained on pp. 351–369.

7. *Location and Functioning of Thermoregulation Centre**

If was due chiefly to the studies of E. Aronsohn and J. Sachs [561a] and of Ott in 1887 that emphasis was laid for the first time on the hypothalamus as a region of the brain concerned with temperature control. Their observations nevertheless remained unnoticed until 1912, after Isenschmid and Krehl[682] had demonstrated in rabbits that, even after removal of the cerebral cortex and corpus striatum, the animal retained a nearly normal ability to regulate its body temperature despite a wide range of changes in environmental temperature. As removal of part of the brain down to the mesencephalon (the second of the embryonic cerebral vesicles) prevented temperature regulation, it was concluded that this centre was located somewhere in the diencephalon. Later studies by Keller and Hare[687], Bazett, Alpers and Erb[573] and, especially, Ranson and Magoun[732] showed conclusively that the hypothalamus is absolutely essential for normal temperature control, although it would be a mistake to conclude that anatomically it is a sharply defined area or that it contains the only neural mechanism concerned with this regulating function. In man certain parts of the cerebral cortex may exert considerable influence. For all that, studies by Pinkston, Bard and Rioch[728] suggest that, except for those specific parts of the cerebral cortex no portion of the brain above the hypothalamus seems to play an important role in temperature regulation of the human body.

As was pointed out on p. 204 the hypothalamus is richly supplied with small blood arteries. The supra-optic and paraventricular nuclei of the anterior nuclei (Fig. 37), in particular are pervaded by a dense network of blood capillaries which seem to be able to register the slightest changes in peripheral blood temperature because of variations in osmotic pressure of the blood which, in turn, are recorded by the neurons of those nuclei.

Studies by Magoun, Harrison, Brobeck and Ranson[705] seem to suggest that there may be two fairly distinct thermo-regulative mechanisms in the hypothalamus, *viz.*, a more frontal (rostral) part which prevents overheating

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* The following summary is mainly based on Hensel's publications[672] and the recent experiments performed by T. H. Benzinger [584–586], Head of the Bio-Energetics Division of the Naval Medical Research Institute at Bethesda, Md. (U.S.A.). I wish to avail myself to this opportunity of thanking Dr. Benzinger and the editor of the Proceedings of the National Academy of Sciences for permitting me to reproduce several of Dr. Benzinger's illustrations and to quote considerable parts of his article.

and a posterior (caudal) part which protects against cooling. Ranson and Magoun[732] showed that electrolytic lesions of the *caudal part* of the hypothalamus (mammillary bodies, see Fig. 37) in cats and monkeys produce poikilothermic conditions; animals fail to sweat or pant when warmed and do not shiver when cooled. Lesions of the *rostral parts* above and in front of the optic chiasma and below the preoptic and supra-optic regions (see Fig. 37) prevent the animal from protecting itself from overheating. The animal fails to pant or sweat if heated and develops a hyperthermia, but it is still able to regulate against cold stress. Further evidence that this rostral section controls the heat loss mechanism was shown by Magoun *et al.*[705] by heating this part of the brain through 2 electrodes by a high-frequency, low-voltage, alternating current. Warming of the area of the optic chiasma, preoptic and supra-optic regions rapidly brought on panting, sweating and cutaneous vasodilatation due to inhibition of the normal orthosympathetic discharges. The further pathways of this cooling mechanism run through the lateral hypothalamic areas. Control of chilling seems to be mainly located in the caudal parts (mammillary body, etc.).

Benzinger pointed out that like any regulatory mechanism in physiology, heat regulation requires three different mechanisms: sensory receptor organs, effectors and a co-ordinating centre.

Presence of specific sensory receptor organs

These organs should be able to register the thermal changes of the environment and to produce directly or indirectly certain nerve impulses commensurate with the magnitude of the thermal stimulus. Various studies suggest the existence of a number of such thermal receptors.

(1) Studies by Blix and Donaldson (see p. 210) suggest the presence of thermal receptors in the skin (Krause endbulbs for cold and Ruffini organs for warmth). Both change in temperature and electric stimulation of the nerve endings of these receptors create a temperature sensation (see page 210).

(2) R. H. Kahn[685a] discovered that intracranial rise in temperature activates the heat loss mechanism (see also above experiments by Magoun *et al.*).

(3) C. von Euler[620a] was able to show that artificially induced changes of temperature in the preoptic and supra-optic regions of the hypothalamus in cats create very characteristic "slow temperature potentials", which indicate the existence of receptor cells which can transform thermal energy into electric energy like a retinal cell changes light energy into an electric potential.

Presence of one more effectors (i.e. organs which affect an organism's response to a stimulus)

At least three mechanisms are known to respond to a change in body temperature, *viz.*,

(a) *Increased metabolic rate* in response to cold stress, as demonstrated for the first time by M. Rubner in 1900 (see also p. 213).

(b) *Secretion of sweat* in response to heat stress (see p. 216), followed by evaporation and cooling.

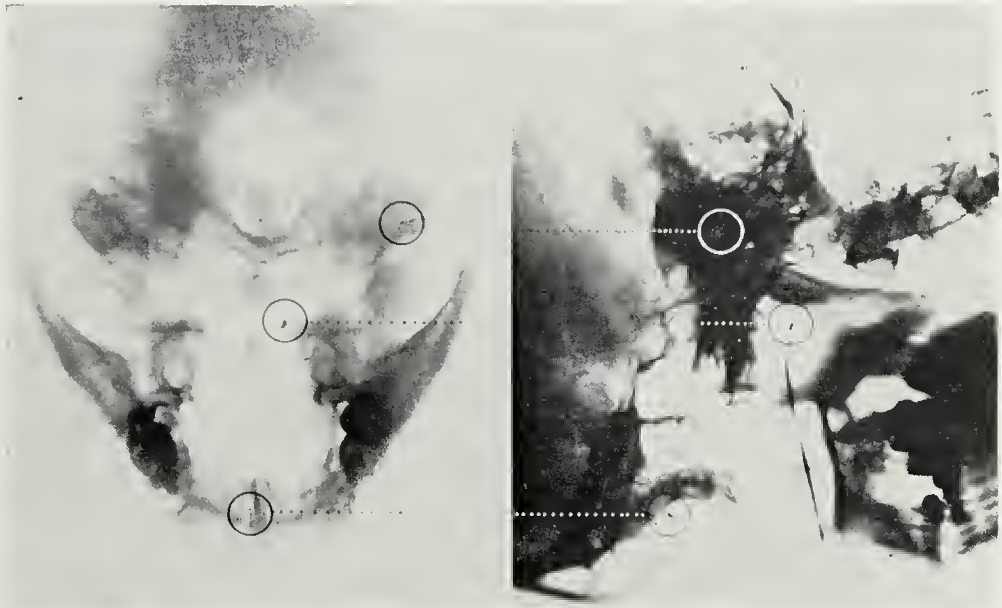
(c) *Increased blood flow* after heat stress, as a heat transferring component from the interior of the body to the skin.

Presence of a co-ordinating centre

The function of the hypothalamus as a co-ordinating centre has been described above. Until recently, it was assumed in most physiological publications that changes in environmental temperature were recorded by the thermoreceptors of the skin and the stimuli being transferred to the hypothalamus through nerve connections. Recent experiments by Benzinger, in which he acted as a subject himself, have demonstrated that this concept is not correct. Benzinger developed a method in which changes in internal temperature of both the skin and the brain, as a result of changes in environmental temperature, were recorded at the same time.

The evidence of the following experiments is that the skin temperatures play only a passive part in thermoregulation.

(1) *Thermocouple recordings of hypothalamic temperature.* The hypothalamic heat centre was chosen as the internal site of temperature measurement. With the assistance of a surgeon (G. W. Taylor), a thermocouple of 36-gauge twin wires of copper and constantan was introduced into the external auditory canal of the subject (T.H. Benzinger). The thermocouple junction was placed in the ear at the tympanic membrane. Benzinger was able to show experimentally that the temperature measured at the tympanic membrane represented *cerebral and therefore also hypothalamic temperatures.* The following experiments were carried out to demonstrate this fact. It is known that rectal temperatures often deviate widely from cranial measurements. In collaboration with a surgeon, thermocouples were placed at the anterior outer wall of the sphenoid sinus (air space in the cranial bone above the nose), at the base of the skull in the anterior ethmoidal region (bone in front of sphenoid and below the frontal bone) and in the nasopharyngeal recess of Rosenmueller (the thermocouple sat on the stern of the internal carotid artery). In Fig. 42 the X-ray picture gives the exact location of the electrode. After ingestion of ice, the temperature curves showed



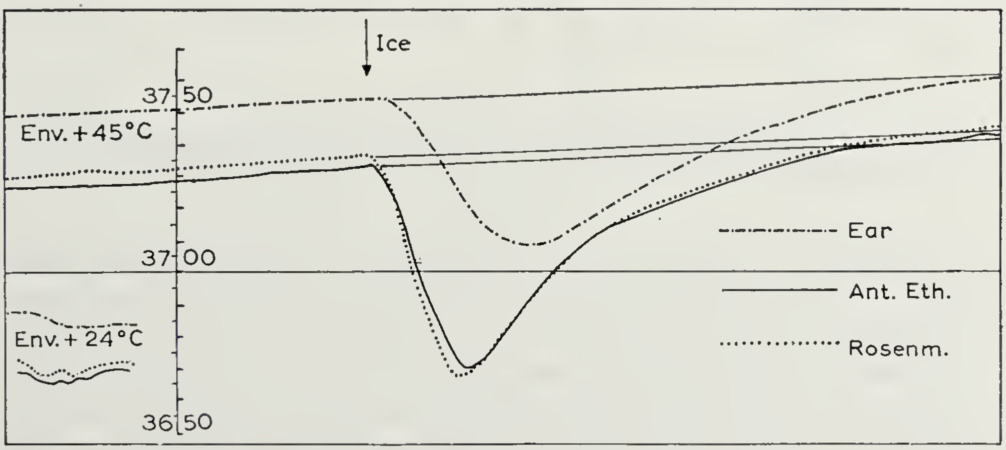


Fig. 42.
Intracranial measurements of body temperature (after Benzinger[584]). Above: X-rays in lateral and mento-vertical views showing position of thermocouples. Below: Recording taken immediately after X-ray, showing three practically identical responses in quantity at ear, anterior ethmoidal site and Rosenmueller's recess.

that the three groups of temperatures taken at distant sites supplied by the same internal carotid artery agreed within 0.2° C in absolute terms and within 0.03° C in their relative movements. Therefore they also represent hypothalamic temperatures which, unfortunately, cannot be measured directly (for further details see ref.[584–587]). The tympanic membrane produced a similar curve, only the response was less rapid after cooling owing to slower

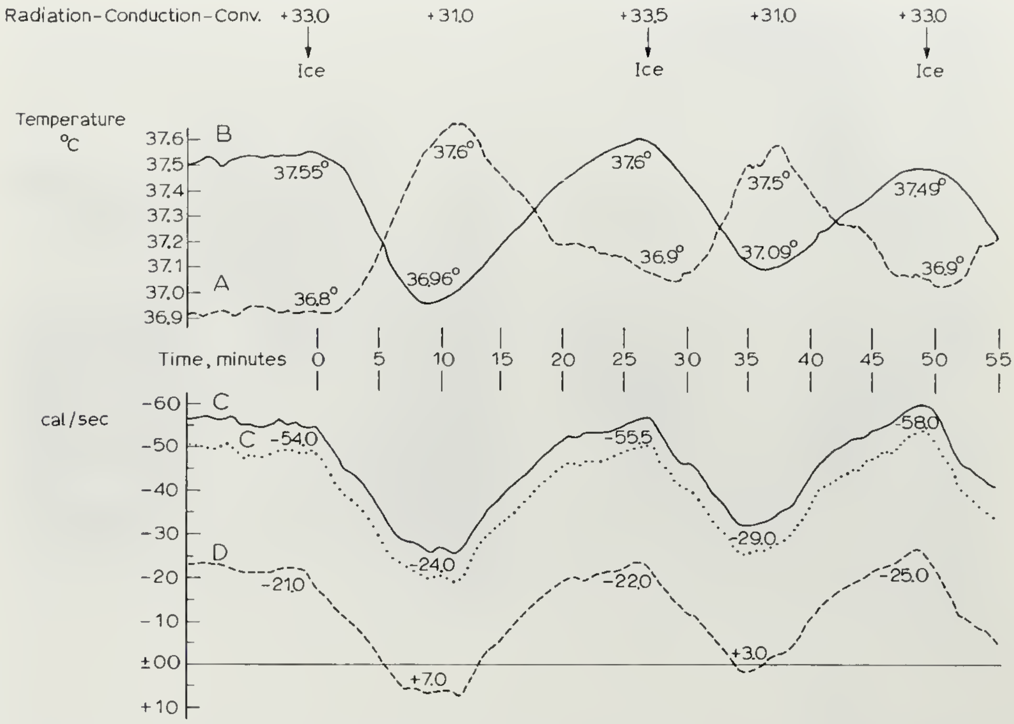


Fig. 43.
Sweating, a response to internal cranial, not skin temperature (after Benzinger[584]). A: skin temperature; B: internal cranial temperature; C: sweating; D: heat loss.

blood circulation through bone and cartilage. The temperature of the membrane is also higher because evaporative cooling occurs at the other three wet locations. The skin temperature was recorded at ten places together with these brain temperature recordings.

(2) *Simultaneous recording of heat loss, sweating, and cranial and skin temperature.* The calorimetric method of Benzinger and Kitzinger has been described on p. 219. It enables the loss of heat, rate of sweating and peripheral blood circulation in man to be recorded precisely, rapidly and continuously. Fig. 43 gives the result of an experiment during which cyclic changes in internal cranial temperature, rate of sweating and skin temperature were produced by the repeated eating of ice (450 g). The temperature curves show that heat loss and the rate of sweating follow the cranial temperature and not the skin temperature. The heating of the skin after the ingestion of ice was caused by reduced sweating in response to the stimulation of the hypothalamus by cold blood. The environment in this experiment was hot (+ 45° C).

(3) *Quantitative mechanism of human hypothalamic heat regulation by sweat gland activity.* On eight different days in October and November 1958 a subject 33 years of age rested or worked at either one or two levels, 6 or 12 cal/sec; in the "gradient calorimeter" (see p. 219) at environmental temperatures of + 10, + 15, + 20, + 25, + 30, + 35, + 40 and + 45° C. Each state of rest or exercise was maintained until, after an hour or more, all thermocouple and calorimetric observations had reached steady levels.

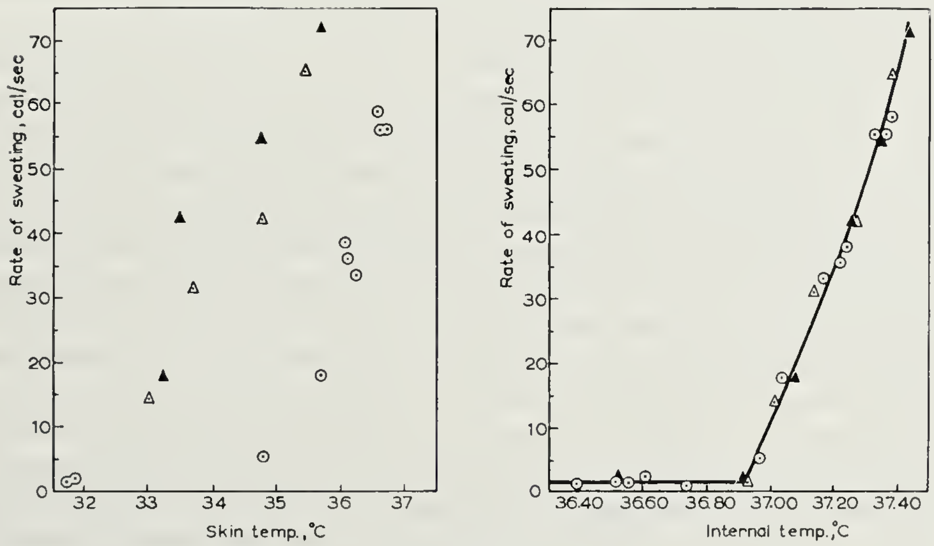


Fig. 44.

The quantitative mechanism of human hypothalamic heat regulation by sweat gland activity (after Benzinger[584]). ⊙: rest; △: exercise, 6 cal/sec; ▲: exercise, 12 cal/sec.

In Fig. 44 (left part) the rates of sweating were plotted against skin temperature. A line drawn through the points of observation at rest show a reproducible relationship between skin temperature and rate of sweating. However, this is not a true stimulus-response relationship, because during exercise the rate of sweating (triangles in Fig. 44) fell widely off the rest-curve. This dissociation is due to increased metabolic activity through exercise, which affects skin temperature very little but changes internal temperature very much.

In Fig. 44 (right part) the inseparable relation between internal cranial (hypothalamic) temperature and rate of sweating is consistent for both work and rest even with most drastic changes of skin temperature.

These various experiments go to prove that the *anterior hypothalamus* (supraoptic and paraventricular nuclei) *is not merely a site of synaptic interconnec-*

tions but a thermal sensory organ with neurons for temperature recording, comparable to the retina as sensory organ for light. The response sensitivity of the "temperature-eye" is, according to Benzinger, an increase of one cal/sec of sweat evaporation and 0.25 ml/sec of cutaneous circulation to every increase of hypothalamic temperature by 0.01° C.

It has also been shown by Benzinger that *no special pathways connecting thermoreceptor cells of the skin via the thalamus with the hypothalamus seem to be required* to account for temperature regulation. Benzinger's observations are supported by recent studies published by Hensel *et al.*. Hensel and Krüger[661] introduced a silver thermode 1 mm thick in the frontal part of the hypothalamus of a cat. The thermode was cooled with a fluid, the blood flow in the ear of the cat being recorded at the same time. It was found that the cooling of the frontal part of the hypothalamus coincided with vaso-constrictions of the ear. A fall in temperature of 4° C causes a 50% decrease in blood flow in the ear. The degree of constriction runs parallel to the drop in temperature of the hypothalamus (directly recorded with a thermocouple). Only the initial condition of the cat affects this constriction to any considerable extent. If, for instance, a reflex vasoconstriction of the skin has occurred before the experiment, the central cooling of the hypothalamus no longer affects the blood flow. Hensel also observed fairly rhythmic *changes in hypothalamic temperature and blood flow* under constant environmental temperature conditions of 23° C. The changes in blood flow usually followed within 1 to 5 seconds of changes in temperature recorded in the hypothalamus. An increase in hypothalamic temperature is recorded a few seconds after vasoconstriction and a fall in temperature soon after dilatation. The amplitude of these temperature changes lies between 0.05 and 0.2° C, the frequency of changes is 1 to 2 minutes. Whereas cooling of the frontal part of the hypothalamus is followed by vasoconstriction, Hensel was able to show that cooling of the front paws of the cat (placed in water of 19° C) causes a strong reflex vasoconstriction followed by a rise in hypothalamic temperature of 0.6° C. After retraction of the paws from the water and slight warming, vasodilatation occurs followed by a fall in hypothalamic temperature. Peripheral heating of the paws in water of 40° C gave the opposite result. Vasodilatation and increased blood flow occurred after 5–20 seconds together with a drop in hypothalamic temperature of 0.05–0.4° C. The vasoconstriction and vasodilatation in both experiments continue till the rise or fall in hypothalamic temperature has reached a certain value. The changes in rectal temperature follow the hypothalamic changes only at a lower temperature level (about 0.3° C). The rectal changes began about 10 seconds after those of the hypothalamus.

So far we have discussed only the thermoregulative centre of the internal body. The *sense of temperature in the skin,* with its afferent impulses (*i.e.* conducted toward the centre of the body) and the thalamocortical neural mechanism in which these impulses are received and translated into highly coordinated motor activity, represent a *second important autonomous peripheral thermoregulation system.* The physiological mechanism of this cutaneous receptor mechanism has been a special object of study in recent years by Hensel *et al.* and Hardy. It is this *conscious temperature perception* in the human skin which assists the body to protect itself from extreme thermal stresses. However, as far as precision is concerned, the hypothalamic *involuntary* mechanism is far superior.

Studies by Hardy and Hendler[645], using heat radiation recorders, demonstrated that very small temperature changes are necessary to initiate cutaneous temperature sensations. This observation seems to support the theory put forward by Weber (1846) stating that it is not the temperature *as such,* but only temperature *change,* which lead to stimulation of the thermoreceptors. According to Hardy, the threshold for warmth sensation was found to be an increasing skin-temperature change rate of between 0.001 and 0.002° C/sec, that for cool sensation being a decreasing rate of between 0.005 and 0.006° C/sec.

It has often been observed that when skin temperatures did not change and the subject was asked to express his feelings, his report always tended to be a repetition of his sensations reported about 10 seconds previously. The observation that, after the removal of a cold object which has been in contact with the skin for 30 seconds, the cold sensation may continue for almost 20 seconds (although the skin becomes warm again) is another example of an apparent discrepancy in Weber's theory (see further below).

Continued rapid fluctuations in skin temperature are not usually accompanied by temperature sensations. Hardy suggests that this may be due to the time required for thermal change induced at the skin's surface to reach the thermal receptors below that surface. According to Hensel, this time factor in thermoreceptor excitation may be of the order 20 msec. The depth of thermoreceptors below the surface is about 0.18 mm. According to Hardy, the thermal inertia of the surface tissues separating the skin surface from the thermal receptors may act as a filter to protect the peripheral nervous system from a continuous barrage of rapidly changing surface temperatures.

It is outside the scope of this publication to discuss the deeper physiological mechanisms involved in thermoreceptor sensation in greater detail. The interested reader is referred to ref.[672]. Only a few general remarks will be made in this section. It has been pointed out (see p. 210) that Hensel *et al.*[665-669, 672, 673] were able to record the action potentials from single specific temperature fibres of thermoreceptors in the sensory nerves of cats and dogs. They showed that at a constant temperature T_1 a simple fibre of the receptor has a steady discharge with a certain frequency F_1. If the temperature is lowered to T_2, the receptor discharge frequency suddenly jumps to a high value (known as "*excitation overshoot*") and then declines to a new constant level F_2, which is higher than F_1. This discharge of cold fibres during sudden cooling may increase from 10 to 140/sec. If the temperature is brought back to the first level T_1, the discharges momentarily cease and return finally to the initial value F_1. The "excitation overshoot" becomes smaller, when the temperature is changed more slowly; also the maximum is reached at a later moment.

The above phenomenon of "*persistent cold sensation*", after the environmental cold stress is removed, has been studied in recent years notably by Hensel *et al.*[672]. Hensel recorded the action potentials from the cold fibres* in the lingual nerve of the cat. Hensel showed that below a temperature of 22°–23° C a persistent stimulation of cold receptors is possible at completely constant intracutaneous temperature. When the tongue is warmed from 10° to a temperature below 22° C, the cold impulses persist throughout the whole period of warming or even after establishment of a constant temperature of 21° C. These cold sensations disappear above 22° C. Judging by the experiments conducted by Hensel, this after-sensation of cold is due to a true, adequate stimulation of the cold receptors by the prevailing low temperatures. Below a certain temperature, cold impulses seem to be always present, independently of whether the temperature rises or falls. The discharge frequency (being max. 10/sec) depends on the absolute receptor temperature. These observations seems to be in contradiction with the theory of Weber that only a rise or fall in temperature creates an adequate stimulus for thermoreceptors. However, it should also be realized that, even during a general period of temperature constancy or rise, small air currents may create short periods of cooling which last only seconds or fractions of seconds (see also p. 36).

The foregoing, rather extensive, review of the location and function of the principal thermoregulative mechanisms was given because they seem to

* Hensel and Zotterman[665] were able to show that the specific cold fibres in the different nerves of mammalia consist of myelinated fibres of 3–6 μ diameter and with a thermal conduction speed of 10–25 m/sec.

play a fundamental part in all bioclimatological phenomena known so far. Only a deeper understanding of these various mechanisms, which require considerably more research, may help us in the future to understand the fundamental physical processes involved in meteorotropism.

8. *Mechanism of Acclimatization*

Despite the various mechanisms described above, which protect the body against excessive heat or cooling (such as sweat secretion, peripheral vasodilatation or constriction, etc.), sudden thermal stress during cold or heat waves usually cannot be compensated immediately by these regulating processes and it may take a few days or more before the body can adapt itself to these changed environmental conditions. Experiments carried out by a series of research workers suggest a number of interesting physiological phenomena related to the problem of thermal acclimatization. The problem will be discussed more fully in a later section by Professor Macfarlane, but a few general remarks will be made in the present section.

(1) Acclimatization to heat is probably not a reflex but a *complicated process of slow physiological adjustments* (Glaser[627]).

(2) The level of deep and superficial body temperature at which thermal balance is achieved *depends on the preceding thermal environment* (Glaser[631], Wilder[559]). The effect of previous thermal stress may persist for very long periods.

(3) Previous exposure to thermal stress *facilitates adaptation at a later period of climatic stress* (Glaser[637]). Glaser and Whittow demonstrated that pain or rise in blood pressure which normally accompanies the immersion of hand in icy water, diminishes or can be lost after repeated immersions in the course of a number of days[636, 637]. People exposed to strong fluctuations of environmental temperature have a very efficient control of the skin temperature and can easily adapt to cold (Goldby, Hicks, O'Connor and Sinclair[745]). The same is true for oxygen adaptation at high altitudes (Hunt[1612]). As this rule applies to various other adaptational processes, the primary cause must not be sought in one particular organ but in certain brain centres.

(4) With a given stimulus *higher sweat rates can be elicited in the summer than in winter* during heat acclimatization (Winslow, Herrington and Gagge[786]). In other words, adaptation to heat stress is easier in summer than in winter. For cold stress it is the reverse. This may explain why the effect of the same meteorological factor or group of factors is different in summer from what it is in winter. An influx of cold polar air or a cold front after a

period of heat adaptation will have greater effect than after a previous cold period.

(5) Experiments by Davis[481] have shown that *repetition of stimuli* (as experienced during acclimatization) may be accompanied by *gradual changes in responses to those stimuli,* a process described as *habituation.* It also explains the change in effect of drugs if applied at regular intervals (Glaser and Newling[632]). Konorski[508], Young[560], Eccles[485] and Glaser[631] were able to show that habituation is probably caused by permanent ("plastic") changes of the nerve junctions as a result of previous stimuli. (see p. 183).

(6) *Application of vitamin C increases the resistance to cold stress and facilitates adaptation* (Dugal and Thérien[615]). It depends on the ascorbic level in the tissue, especially in the adrenals (see p. 279).

Before complete heat acclimatization has taken place, the following physiological processes are observed:

A sudden *heat stress* (due, for example, to influx of warm tropical air masses) causes a rise in body temperature and in extreme cases a rise of basal metabolic rate, increase of respiratory ventilation, rise of blood pH, increase in pulse and circulation rates, usually a fall in arterial pressure, increased sweating, dilatation of the arterioles and capillaries of the skin, increased blood volume, decreased haemoglobin content, usually a decrease in leucocytes and granulocytes, increase in blood sedimentation rates, decreased diuresis, usually fall in pH of urine, increased chlorine secretion, decreased 17-ketosteroid secretion (sudden heat waves may create a mental stress condition with increased 17-ketosteroid secretion during the first 2 days), increased skin permeability and decreased capillary resistance. *Cold stress* has similar, but reverse effects.

In 1939 Radsma[542, 543] studied in Java the physiological effects produced in inhabitants of the tropics by a short exposure to a cool environment, in particular the effects of moderate differences in cooling power on the human body. These conditions may bear more directly on the problem of acclimatization of man to the tropics than many of the published tropical chamber experiments with temperatures far above 30° C whereas the temperature at Djakarta (Java), for instance, is usually less than 28° C. Radsma also pointed out that acclimatization to tropical climate cannot be solved by experiments of a few hours or even a day in a cool or tropical chamber, because a continuous stay in the tropics may change the physiological reactivity to thermal stress. Radsma used as his subjects a large number of Malay servants, Malay students, Dutch students and Dutch doctors. The following differences in physiological pattern were found between resting subjects who stayed for a whole morning either in an ordinary tropical chamber (dry bulb temperature 29° C, relative humidity 70%) or in a cooled chamber (temperature 22–24° C, relative humidity 65–70%):

Respiratory metabolism: slightly lower in the cool room
Rectal temperature: practically the same in both cases
Urine volume: larger in the cool room
Water losses through skin and lungs: practically the same in both rooms
Blood volume: decrease in the cool room
Pulse rate: higher in the warm room
Blood pressure: significant increase after prolonged sojourn in the cool room at 21° C
Oxygen saturation of blood in the cubital (fore arm) *vein:* 38.1% in the cool room against 58.5% in the tropical room
Minute volume of blood circulation (*i.e.* CO_2 output/min collected in the expired air): same in both rooms
Alveolar tension and respiration rate: usually slightly higher in the initial stage in the cool room
pH of blood: no difference
pH of urine: in the cool room 0.27 higher than of that excreted in the warm room

As stated above, in cases of a severe heat or cold stress these various physiological processes preceding acclimatization are more pronounced.

It seems that improvements of the various physiological dysfunctions during thermal stress are due mainly to cardiovascular adaptations. Various authors believe that improvements are the result of increased blood volume (see p. 322). Seasonal variations of 22% in blood volume from winter to spring have been reported by Bazett[570]. Conn[601], Weiner[779] and others support the view that the endocrinal system is responsible, at least partly, for the adjustment and acclimatization to high temperatures. The excretion of the anti-diuretic hormone by the pituitary, of aldosterone by the adrenal gland, and decreased thyroid activity have been considered to be particularly important factors in this process.

9. *Biological Effect of Air Conditioning*[795–806]

Air conditioning can be defined as the control of the temperature, moisture content and purity of the air in a room or building in order to create a comfortable environment for the occupants.

The main principle in air conditioning is the passing of an air current (at normal or pre-heated temperatures) through a humidifying chamber in which a fine water spray is discharged. Soluble gases and suspended particles are removed and a clean water-saturated air current leaves the chamber. A thermostatic device controls the temperature at which the air leaves the spray chamber and also its water vapour content. In order to reduce the amount of water vapour, the air should be cooled below its dew point. One method is to cool the air through an *air washer* (for further details see Bedford[795, pp. 320–334]). The reduction of humidity facilitates sweat evaporation during high temperatures and increases our comfort in humid tropical climates considerably.

Influence of humidity on our mental performance

This was clearly demonstrated by the experiment of Mackworth[704] who tested 11 physically fit, competent wireless telegraphy operators in hot and moist atmospheres. They had to record morse messages over the telephone. Whereas at a dry bulb temperature of 85° F the average number of mistakes per subject per hour was 12.0, it increased to 15.3 at 87.5, to 17.3 at 100 and to 94.7 at 105° F. Exceptionally skilled men did not begin to deteriorate until the temperature exceeded 100° F.

Influence of air conditioning on health

It was pointed out on p. 230 that to enter a cooled building on a hot summer's day may cause considerable chilling and may even lead to disease. Various research workers have assumed that air conditioning may affect the health of people living many hours of the day in air-conditioned surroundings. The effect of air conditioning on health, both on land and at sea, has, however, received very little scientific study up to date.

(1) *Possible effect of air conditioning of rooms and buildings on land.* In 1932 McConnell[798] studied the difference in disease of the staff of the Metropolitan Life Insurance Company at New York who worked partly in a new air-conditioned building and partly in an older office without cooling facilities. Sex, age distribution and economic status of both groups were about the same. Although the air conditioned building was considerably more comfortable to work in, there was no significant difference in either respiratory diseases or non-respiratory illnesses between the two groups. Absenteeism was also the same. On the other hand, this result was not confirmed by other research workers. The very constant micro-climatic conditions may have favourable biological effects in certain instances (*e.g.* asthmatics), but the lack of turbulence in the air is not invigorating. Moreover, sunshine is often excluded from air conditioned buildings. The effect of the lack of sunlight will be discussed more extensively on p. 261. All in all, the study of the effect of air conditioning on human health is a very complicated problem and considerably more research is required before a definite conclusion can be drawn.

(2) *Possible effect of air conditioning of ships at sea.* Smith[747] described a

4 year study (Oct. 1948–Sept. 1952) of sickness reported to the British Royal Navy based on 1855 sickness forms collected from 104 different warships, of which 40% were from large ships and 49% from smaller ships. The following results were obtained:

(1) Minor sickness increases during hot weather in all classes of ships. Skin diseases in particular showed a pronounced increase with rising environmental temperature.

(2) When the environmental temperature at noon on the upper deck of the ship was 60° F about 3% of the ship's company were on the attending list; with 80° F, 5%; with 90° F, 9%.

(3) A comparison of the incidence of sickness on hot stations in the same ships, before and after installation of air conditioning, showed that after air conditioning was introduced the total attending list was reduced by 39%; the incidence of skin diseases and injuries decreased by 43 and 46% respectively.

(4) In the Persian Gulf, with air temperatures above 90° F, the attending list in ships with air conditioning was 7% against 11% in ships without air conditioning. Skin diseases were reduced by almost one half.

(5) In cold weather upper respiratory diseases tend to increase. In very cold weather they represent 23% of the total attending list, against 7% in very hot weather.

Whereas air conditioning in very hot climates seems to have a benificial effect, in temperate climate the effect may be less favourable. L. L. Stanley reported that in the *S.S. Lurline,* travelling between Hawaii and San Francisco during 1951, passengers were complaining after the ship was air conditioned. People felt "as if they were coming down with colds"; they complained of running noses, sore throats and a feeling of stuffiness. Some people felt cold all the time. Several cases of sudden asthma attacks were observed.

Also during trips in tropical zones in passenger ships people often have minor complaints, particularly if only the dining room or a reading room is air-conditioned. Under these conditions the human body is continuously subjected to great differences in temperature moving from deck to cabin and dining room. This causes a constant stress on the thermal regulation mechanism of the body. Whereas the crew may gradually acclimatize to these rapidly changing temperatures (and some of the crew may not even live in air-conditioned quarters), the passenger's sojourn on board is usually too short for them to acclimatize and they may therefore suffer from various diseases as a result of reduced thermoregulation capacity.

10. *Effect of Temperature on Joints and Fluid Viscosities*

The influence of temperature on joints and tissues is a matter of prime importance in the study of the influence of weather and climate on rheumatic diseases. An interesting study on this subject was published in 1957 by Fisher *et al.*[623].

Notwithstanding numerous investigations into thermal phenomena in the human body, surprisingly little is known of the actual physical processes involved. A careful analysis of the problem, however, makes the difficulty of studying these problems on a truly physical basis clear, as may appear from what follows. G. W. Molnar[623] worked out a formula for heat transfer through the hand, which, in a simplified form, reads: heat input $\pm$ storage $=$ heat output. In more physical terms Molnar's formula runs thus:

$$\{Mt + B\,(T_a - T_v)\rho_1 C_1 t\} + \{\rho_2 C_2 V \Delta T_m\} = \{H(T_s - T_e)At + \lambda k(p_s - p_e)At\}$$

where M = rate of heat production, t = time, B = rate of blood flow, T_a = arterial temperature (*i.e.* temperature in vessels carrying blood away from the heart), T_v = venous temperature (*i.e.* temperature in blood vessels returning blood to the heart), ρ_1 = blood density, C_1 = blood specific heat, ρ_2 = density of hand, C_2 = specific heat of hand, V = volume of hand, T_m = mean temperature of hand, H = heat transfer coefficient for conduction, T_s = skin surface temperature, T_e = environmental temperature, A = surface area, λ = latent heat of evaporation, k = mass transfer coefficient, p_s = vapour pressure of skin surface, p_e = vapour pressure of environment.

This formula clearly indicates that at least 19 factors are involved in an accurate thermal study of heat transfer through the hand or other parts of the body, which may explain the relatively small scientific progress made so far. Nevertheless, a number of interesting empirical observations have been made. J. Hunter[623, pp. 6–15] studied the effect of cold on *joints** and fluid viscosities. The following observations were made:

(1) Before the experiment the rectal temperature was highest, followed by skin, muscle and joint temperature (lowest). Twenty minutes after exposure to low environmental temperature the rectal temperature had not changed, but the skin temperature was falling, the muscle temperature much more and the joint temperature was falling most of all.

(2) After the subject had returned to a room with the same temperature

* A joint, which is the site of junction between two or more bones admitting the motion of one or more of the components, consists of a tissue space lined by modified connective tissue cells. The inner part is provided with blood vessels, lymphatics and nerves. The pressure to which a joint is subjected affects the exchange between the blood and the synovial fluid, the lubricating joint fluid.

as that preceding the experiment, the joint temperature was still falling and reached a point lower than the lowest temperature recorded in the joint during the experiment. In other words, the joints exhibit a prolonged recovery period.

(3) The fall in temperature is accompanied by a decreased cellular permeability, increased resistance of the joints to movements and a decrease in the maximum speed with which the joint can be moved. This increase in force required to produce a minimal detectable movement was measured by Hunter in the knee joints of 20 cats. The same technique was used to study the flexural rate of the index finger at various temperatures.

Hunter pointed out that an analysis of a series of X-ray photographs of the motion of the knee or any similar joint (*e.g.* the interphalangeal joints of the fingers) clearly demonstrate that these joint movements can be compared mechanically with a sliding movement. Therefore frictional forces become important. The lubrication of human joints takes place by means of a fluid film, the *synovial fluid**. Therefore the sliding movement depends to a considerable extent on the viscosity of this fluid. As stated on p. 316, the viscosity of serum increases with increased protein concentration, adrenalin secretion, mental stress, etc. Hunter was able to show for bovine synovial fluid that the viscosity is directly proportional to the mucin content, which in turn may depend on the pH of the fluid (more mucin being dissolved in alkaline fluids). With falling temperature the viscosity of synovial fluid with a high percentage of mucin increases considerably more than with low mucin content. The striking similarity between curves indicating the change in viscosity with falling temperature for various mucin concentrations of the synovial fluid and the curves indicating the change in force required to produce a minimal movement of the knee of cats suggest that the joint movement is closely related to the physico-chemical characteristics of the synovial fluid.

The foregoing summary indicates that during winter (with increased protein content of the blood) and sudden cold stress (increased peripheral adrenaline secretion) increased viscosity of the synovial fluid is to be expected. This, combined with reduced membrane permeability of cells (controlled

* It is usually small in amount, *e.g.* 0.5 cc in a normal human knee joint. It is a viscous slippery fluid owing to the presence of mucin (about 0.14%) and other proteins (about 2%). *Mucin* is a glycoprotein, like albumin and globulin, secreted by the mucous membranes, which is precipitated by acids and redissolved by alkalies; it is not coagulable by heat. The low protein content of the synovial fluid as compared with blood plasma (8%), the lack of fibrinogen and lack of capacity to clot distinguish this fluid from blood serum. However, urea and uric acid concentrations are the same. The exact origin of the synovial fluid is not known but most likely it is the liquid matrix of connective tissue.

by corticosteroids and adrenaline, see p. 335), may increase the resistance of the joints to movements and cause insufficient removal of metabolic waste products, such as uric acids, etc., from the joints. As all the processes discussed are controlled largely by our thermoregulation mechanism, inefficient functioning of this system with prolonged recovery may be one of the causes of progressive dysfunction of the joints, which may eventually culminate in rheumatic diseases (see p. 555).

11. Effect of Temperature on Adrenal and Thyroid Activity and Diuresis

In later sections it will be pointed out that cold stress creates hyperthyroidism and hypertrophy of the adrenal cortex, increased 17-ketosteroid secretion and diuresis. For further details we may refer to pp. 269, 279, 280 and 334. As the degree of response of these various processes to environmental changes in temperature depends on the efficiency of the thermoregulative mechanism and considering the fact that the thyroid and adrenal glands control a great number of important physiological processes in the body, it is evident that any disturbance of the thermoregulative mechanism may have serious repercussions in the body as whole.

12. Effect of Thermal Baths on Oxygen Exchange and General Circulation

On p. 330 it was pointed out that according to various authors (*e.g.* Zimmermann) sulphur baths, thermal baths, sauna baths, etc. may have a stimulating effect on the adrenal cortex, causing an increased 17-ketosteroid secretion.

Other important effects of thermal baths were described by Bazett *et al.*[575], *viz.*, the effect of sudden changes in water temperature on the oxygen exchange and general circulation. For example, a person taking a sauna bath, after the hot steam bath is suddenly cooled in cold water. During the first stage, when the water or steam temperature is raised through 40° C, the following physiological changes are observed: rise in rectal temperature of almost 3° C and peripheral dilatation of the arterioles; in the early stages particularly, the cardiac output increases considerably, the blood pressure is usually reduced, the pulse rate increases and in later stages the oxygen consumption may increase and the peripheral resistance is lowered. When the subject enters a water bath of less than 32° C it usually causes shivering and peripheral constriction of the arterioles; the cardiac output is usually reduced, blood pressure is raised, the pulserate slows down, the oxygen consumption usually increases considerably during the initial sudden cooling (but soon reverts to normal), and the peripheral resistance increases

The steam bath and profuse sweating cause dehydration, this effect being stronger in winter than in summer. The increase in cardiac output after cooling is more pronounced in summer.

This summary brings out clearly the highly stimulating effect of thermal baths, the results being different in different periods of the year. In view of the very heavy stress imposed created by these baths, subjects suffering from a weak heart or poorly functioning kidneys should never take them baths without the consent of their medical adviser. For further details see p. 648 (Balneological treatment).

13. General Effect of Temperature on Disease

It is evident from the summary of the effects of thermal stress on various physiological processes that if a certain part of the body has reached the morbidity limit, the thermal stress set up by sudden changes in the meteorological environment may be responsible for a morbid condition of parts of the body or the body as a whole. This morbid condition may be directly due to a dysfunction of important physiological processes (heart function, respiration, etc.) or indirectly as a result of lowered resistance to environmental stimuli, such as infectious micro-organisms and so forth.

The influence of thermal stress on various complex pathological conditions will be discussed more fully in the following chapters, but a few general phenomena will be discussed briefly in the present section.

Influence of thermal stress on industrial absenteeism due to sickness

In 1947 De Groot[605], industrial medical adviser to the Steelworks at IJmuiden (the Netherlands), studied the possible relationship between absenteeism through illness (irrespective of the kind of disease) of male labour and the average environmental temperature. The latter is based on the average of the temperature at 8, 12 and 18 hours, and the minimum daily temperature. From these daily averages, weekly averages were calculated. The following results were obtained: (*i*) During the first part of the year, with temperatures up to 18° C, the absenteeism falls off with rising temperature; above 18° C, absenteeism begins to increase with rising temperature; (*ii*) After the month of September the relationship between absenteeism and temperature was not very clear, in 1947 at all events.

Similar unpublished studies in the Netherlands suggest like relationships, *i.e.* periods of a high percentage of absenteeism in various industries are usually preceded by a drop in temperature and an influx of cold polar air masses.

Influence of thermal stress on mortality

The influence of weather and climate on mortality will be discussed more fully on p. 571. Here, however, a few general remarks will be apt because various studies indicate a statistically significant correlation between temperature and total mortality in a population, more especially between temperature and mortality from arteriosclerotic heart diseases.

In Germany, Spann[3216, 3217] studied the total number of deaths (40,417) in the city of Munich during the years 1950–1953, excluding deaths due to accidents, homicide, suicide, etc. In 39,980 cases the exact hour of death was known.

The following interesting correlations were found: (*i*) Mortality increases during the night and reaches a maximum in the early hours of the morning; it decreases during the day and reaches a minimum in the early evening; (*ii*) The mortality rate is higher in winter than in summer; (*iii*) Mortality is highest during Ungeheuer's weather phase 4 (see p. 25), *i.e.* in periods when there is an influx of new air masses and a steep fall in barometric pressure.

In Great Britain Boyd[3190] studied the relationship between respiratory mortality and meteorological conditions during the winter months of 1947–1954, in the Greater London area and in the rural districts of East Anglia. The observed correlations were essentially the same in both areas. A close association was found between weekly deaths from respiratory diseases in people of 45 years and over, temperature and humidity, particularly if the mortality data were correlated with weather conditions in the preceding week.

In general it can be said that mortality increased with falling temperatures In the London area at temperatures below 32° F bronchitis mortality during heavy fog was three times greater than with light fog. This influence of fog on mortality remains the same only up to a temperature of 36° F. In other words, fog can only be correlated with bronchitis mortality when the temperature is very low.

In the U.S.A., Kutschenreuter[3209] studied the relationships between total mortality and weather in the New York area for the period 1949–1959. The following observations were made:

(1) In the age group 45 and older, mortality is significantly highest on Mondays and lowest on Sundays. In younger age groups this relationship is not very pronounced or is even lacking. Most likely this weekly periodicity is entirely a sociological correlation.

(2) During the influenza pandemic (October 1957–March 1958) no correlation was found between mortality, temperature and precipitation.

(3) However, (*i*) In other periods, in New York, Los Angeles (Cal.) and Cincinnati (Ohio) the total monthly mortality curve shows an inverse

relationship to temperature: *i.e.* highest mortality in coldest months and *vice versa*; the colder the winter the higher the mortality. A sudden increase in mortality may nevertheless also occur during very hot summers; (*ii*) The mortality–temperature relationship obtains only above the age of 24 and below that of 1 year. From 1–24 years no death–temperature relationship was observed, perhaps partly due to the relatively low mortality figures for this age group; (*iii*) In 1910 a secondary maximum was found by Huntington in July. This was primarily due to deaths in younger age groups as a result of lack of pasteurized milk and adequate refrigeration during the hot summers of 1900-1910. This maximum disappeared entirely in the 1949–1959 curves. (*iv*) There is no significant difference between these various curves for the white and non-white segments of the population, except that in the whites maximum mortality occurs in the 65 and over group, in the non-whites in the group of 45–64.

(4) A statistically significant correlation was found in the New York area from January to June, between days of active front passages and high mortality; but in October, after the hot weather of the New York summer, the passage of fronts (accompanied by cooler weather) causes a reduction in mortality, a relationship which is different from Western Europe, where the front–mortality relationship is also observed in the autumn.

Whereas these various studies indicate a general relationship between total mortality and temperature, a more detailed analysis suggests that it is particularly true for mortality from arteriosclerotic heart diseases, as demonstrated by Tromp in the Netherlands[3221], Bundesen and Falk[3191], Mills[3210] and others in the U.S.A. Tromp showed for the period of 1936 to 1958 that, in the Netherlands, mortality from apoplexy, coronary thrombosis and angina pectoris was highest in January–February and lowest around July–August; winters with abnormally low temperatures are marked by very high mortality, warm winters by relatively low mortality; the low summer values are highest during the warmest summers (*i.e.* average monthly temperature exceeding 21° C). Bundesen and Falk found similar relationships in the Chicago area in the period of 1924 to 1926.

In the following chapters considerably fuller evidence will be brought forward concerning the great influence of the thermoregulation mechanism on the pathological processes in the human body.

14. Methods for Testing Thermoregulation Efficiency of the Human Body

Considering the great significance of the thermoregulation mechanism in the body for the maintenance of its general health and in view of the great variety of physiological processes affected by a disturbance of this mechanism, biometeorologists have naturally long been seeking a simple means of testing the degree of efficiency of the thermoregulation mechanism of the human body. Though a definite series of tests has not been devised so far, the following tests may be used as an initial approach to this problem.

Hunting reaction of Lewis

We have seen that if a finger is immersed in iced water (keeping a constant temperature of 0° C), the skin temperature of the finger will fall rapidly to 0°, but 10–15 minutes later, the skin temperature may rise 5–6° C, a phenomenon known as the "Hunting phenomenon". With continued immersion the finger temperature fluctuates slowly between 0 and 5–6° C, which shows up in a graph as a series of undulations. Lewis found that the effect persisted after sympathectomy and peripheral nerve section. Therefore various authors (Lewis, Kramer, Schulze) believe that the vasodilatation and increased blood flow responsible for the rise in temperature, is due to an axon reflex, the more so as this "cold vasodilatation" can be prevented if the finger-tip is treated with novocaine. However, this latter observation was not confirmed by others, including Greenfield. Whelan and Greenfield[638] found that complete section of the nerves to the finger and subsequent degeneration did not prevent the Hunting reaction, although the degree of dilatation was usually less.

Aschoff[562] using a calorimeter, with the whole hand immersed in water, was able to demonstrate that the heat output of the hand in water of 10–13° C was about 25–30 cal/min. If the water temperature is reduced to 6° C, the heat output increased after 10–15 minutes to 150–200 cal/min. The heat output of the finger per unit surface is actually five times greater than that of the whole hand. Aschoff observed during the sudden steep drop in finger temperature that the rectal temperature and nasal mucosal temperature were rising.

Studies by Spealman[751], using a plethysmograph for direct blood flow measurements, also indicated a sudden increase in blood flow of the immersed finger, the flow being comparable with temperatures of 35° C.

According to Kramer and Schulze[688], there are seasonal variations in the Hunting reaction; it is most easily provoked in July and August.

Despite extensive studies of this phenomenon, the deeper mechanism is still unknown, but it is fairly certain that the Hunting reaction is mainly controlled by our highest thermoregulation centres and, therefore, considerable deviations from the normal pattern are a purely empirical indication of a less effective thermoregulation mechanism.

Obviously it is most important to determine first of all the normal picture of the Hunting reaction for each climatological area. Several hundred people of different age groups and sex must be tested at different hours of the day. The normal controls selected should, preferably, be persons not unduly sensitive to hot or cold.

Bedford's air-cooling test

On p. 225 we described the change in skin temperature of the forehead after cooling or heating with an electric fan. The average steepness of the fall and rise of the temperature curve and the total amplitude and degree of asymmetry of the falling and rising part of the curve have to be determined in a great number of normal persons before any conclusion can be drawn.

Water-bath test

The subject should report in the morning before having had breakfast. Clothing, except for pair of shorts, is removed. The subject rests on a bed in a climatic chamber where the air temperature is 20° C and the relative humidity 50%. The skin temperature is recorded at a number of places, *e.g.* forehead, cheek, last phalanx of the first fingers on the right and left hand and on the right and left big toe.

As soon as the skin temperature is stabilized (usually after 10-15 minutes) a reflex vasodilatation of the arterioles of the skin is induced by immersing the feet and lower legs in a warm bath of 45° C. The time between immersing the feet and the first change observed in finger temperature is recorded, but the rate at which the finger skin temperature increases is also noted as well as the final temperature, when equilibrium is again established. After the feet have been lifted out of the bath, the change in temperature during the recovery period is recorded.

The reason for using the finger temperature only is that generally the skin temperatures of forehead and cheek do not change significantly during this experiment.

The same thing should be done with water of 10° C, 5° C and 0° C. The difference between these various curves of the tested subject and those of a large group of normal persons should be compared.

Blood pressure test

Shortly after immersion of the hand in cold water a rise in blood pressure is observed which can be recorded automatically, *e.g.* by using a *sphygmotonograph*. Both the rate of increase and the type of recovery curve of persons with a poor thermoregulative mechanism, are usually different from those of normal subjects.

Blood flow test

Five cubic centimetres of the terminal phalanx, *e.g.* of the third finger of the right hand, are enclosed in a cup of a *plethysmograph* and the changes in blood flow pattern after immersion in water can be studied in normal controls and in the person to be tested.

Habituation test

If the previous tests are repeated daily, the cold response becomes smaller every day and may even disappear. If the experiment is stopped for a number of days, the body is somewhat adapted to the cold stress and even after several days little or no response is observed after a renewed test (Glaser[636, 637]). However, poorly adaptable persons present a different habituation pattern from that observed in normal people.

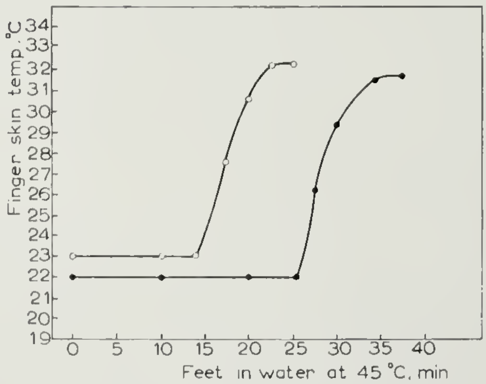


Fig. 45

Prolonged latent period before vasodilatation and rise in finger skin temperature is observed in schizophrenics (as compared with normal subjects after the warm "waterbath test") (after Henschel *et al.* [661]). —o—o—: control group B; —•—•—: schizophrenics.

Diuresis test

It was pointed out on p. 334 that a clearly defined relationship can be observed between temperature (or cooling) and diuresis in a normal subject with an efficient thermoregulation mechanism. When there is a sudden drop in environmental temperature due, say, to the influx of cold air masses, an immediate rise in urine secretion is observed which is accompanied by an increase in 17-ketosteroid secretion (sometimes preceding the increased diuresis by several hours), decrease in chlorine secretion, increase in pH (decreased acidity) and so forth.

As pointed out on p. 538, often an inverse relationship was found in schizophrenics*. During a fall in environmental temperature the diuresis may decrease; with rising temperature it may increase. In mentally normal subjects we generally observe the relationship of increased diuresis during falling temperature, but many deviations from this rule may occur. As this whole phenomenon is closely related to the thermoregulation mechanism, a considerable deviation from the normal temperature–diuresis curve suggests a disturbed thermoregulative process.

The subject to be tested should make an accurate record of his fluid intake for 4 weeks if possible. The daily amount of urine, 17 ketosteroid content, chlorine content, etc. should be determined. These curves should be compared with the average daily temperature and cooling curves.

As diuresis is markedly affected by the adrenal cortex (see p. 332) it is advisable to take an adrenocortical efficiency test, either the *Kepler, Soffer and Gabrilove*[748] or *Oleesky test*[723] before the temperature test. In the Oleesky test the subject is deprived of fluid from the previous evening till the next morning. The subject is asked to drink 1 litre of water within 20 minutes. The urine flow is measured every 15–20 minutes for $2^1/_2$ hours. In adrenal insufficiency the maximum flow will be less than 2–3 ml/min and becomes normal after giving 50–75 mg cortisone. If the patient, after having voided at 8 a.m., can drink 1500 cc (test of Soffer and Gabrilove) he should be able to excrete more than 1200 cc within 5 hours (normally 1200–1900 cc). If a cumulative urine volume curve is prepared (the total volume being determined for each hour) normally the curve rises steeply and reaches a point above 1200 cc, after 5 hours. In cases of Addison's disease (see p. 278), it is about 200–700 cc; with hypopituitarism (Sheehan's syndrome) it is less than 200 cc.

It should be borne in mind that the previous experimental history of the subject is very important in all these tests (Wilder's law, p. 190). Although we shall never find a large number of normal persons with exactly the same temperature and experiences during the period preceding the test, the differences can be reduced to a certain extent by giving the subjects the same meal and by keeping them at least one hour in a climatic chamber in which a certain temperature, humidity and air movement prevail, before the tests are made.

* It has often been reported that schizophrenics are characterized by cold and cyanotic hands (*i.e.* bluish tinge of skin and mucous membranes caused by lack of oxygen). Henschel *et al.*[661] demonstrated during a warm *water bath test* that, once dilatation started, the time course and magnitude of response and the plethysmograph recordings are the same in schizophrenics and normal subjects, but schizophrenics exhibit a significantly prolonged latent period before vasodilatation begins, as compared with normal persons (see Fig. 15). They seem to have either an exceptionally high and persistent state of tonus in the skin vessels or an abnormally high temperature threshold in the hypothalamus.

Subsect. D. THE FUNCTIONING OF DUCTLESS GLANDS

Biometeorological processes are also considerably affected by the functioning of the ductless glands, in particular the *pituitary* (also known as *hypophysis*), *thyroid, parathyroid, adrenal gland* and *pancreas*.

1. The Pituitary Gland (Hypophysis)

General anatomy

This gland, known as the leader of the "endocrine orchestra", consists of a neural and glandular division (see Fig. 46).

The *neural division* is an outgrowth from the floor of the third ventricle (space between the thalami, representing the cavity of the embryonic forebrain). It includes the *pars nervosa*, the *infundibular stem* (or pituitary stalk) and its continuation, the *median eminence*. This part of the pituitary is richly supplied by non-myelinated nerve fibres, which arise in the hypothalamus (supraoptic nucleus, see p. 202). There is also a rich capillary blood supply.

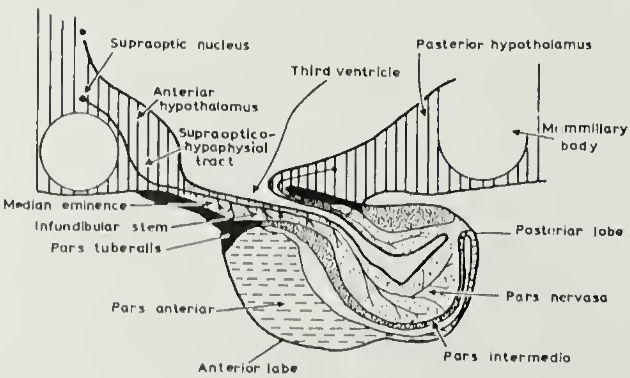


Fig. 46.
Section through the hypothalamus and hypophysis of the cat.
(after. S. Wright, *Applied Physiology*, Oxford University Press, London, 1948, p. 260).

The *glandular division* consists of the *pars anterior* (a large, compact, highly vascular organ, with very few nerve fibres), the *pars tuberalis* (difficult to demonstrate in man; in animals it embraces the pituitary stalk and extends to the hypothalamus) and the *pars intermedia* (a thin poorly vascularized tissue, which in amphibia and certain fishes secretes a hormone causing the expansion of pigment-bearing cells, the melanophores, in their skin). It often invests the *pars nervosa*. The pars nervosa and pars intermedia from the *posterior lobe* of the pituitary. The pars anterior is also known as the *anterior lobe* or adenophysis.

The functions of the antior lobe (see Fig. 47)

They can be summarized as follows:

(1) It controls the growth of the skeleton by secretion of a *growth hormone.* Over-secretion (hyperpituitarism) may cause *gigantism.*

(2) It regulates the activity of the gonads (both in males and females) by secretion of *gonadotrophic hormones* which are glycoproteins. In females two hormones are known: the *follicle-stimulating hormone* (FSH, prolan A), which increases the number and size of the follicles, and the *luteinizing hormone* (LH, prolan B), which acts on the ovaries, controlling the appearance, growth and persistence of the corpus luteum. FSH and LH control the ovarian cycle and liberation of the two ovarian hormones *oestradiol* (perhaps formed by the follicular tissue) and *progesterone* (formed by the corpus luteum). For the study of the possible influence of weather and climate on birth frequency and related phenomena in females these facts are of great importance. In males FSH controls spermatogenesis. Both in males and females it also controls processes which lead to differentiation of the gametes, *i.e.* the ovum and spermatozoon respectively. LH controls the secretory activity of the interstitial cells of the testis.

(3) It influences the growth of the mammary gland during pregnancy and controls the secretion of milk by means of a *lactogenic hormone, prolactine.*

(4) It controls the activity of the adrenal cortex by an *adrenocorticotrophic hormone* (ACTH), *adrenotrophin.* Hypophysectomy leads to cortical atrophy.

(5) It regulates the secretory activity of the thyroid gland by means of the *thyrotrophic hormone thyrotrophin* (a pseudoglobulin). Hypophysectomy leads to atrophy of the thyroid.

(6) It influences metabolism *indirectly* by *thyrotrophin* but also *directly.* Pituitary extracts have the following effects: (*i*) The carbohydrate metabolism is influenced by the *diabetogenic hormone* which stimulates new sugar formation and raises the blood sugar level; (*ii*) The fat metabolism is influenced by the *ketogenic hormone* which mobilizes depot fat and increases ketone body production; (*iii*) The tissue metabolism is influenced by the *metabolic hormone* which stimulates the metabolism of the tissue cells directly (and not indirectly) *via* the thyroid. It is very likely that the three metabolic activities just described are actually due to the *growth hormone.*

(7) The islets of Langerhans (see p. 281) are affected in a complex way. It is found that crude extracts of the anterior lobe of the pituitary may increase the amount of islets tissue. Hypophysectomy causes atrophy of the islets and decreases insulin production. As a result the liver glycogen store is decreased and fats are converted into ketone bodies (*i.e.* β-hydroxy-butyric acid and aceto-acetic acid). Owing to this excessive ketogenesis the blood-

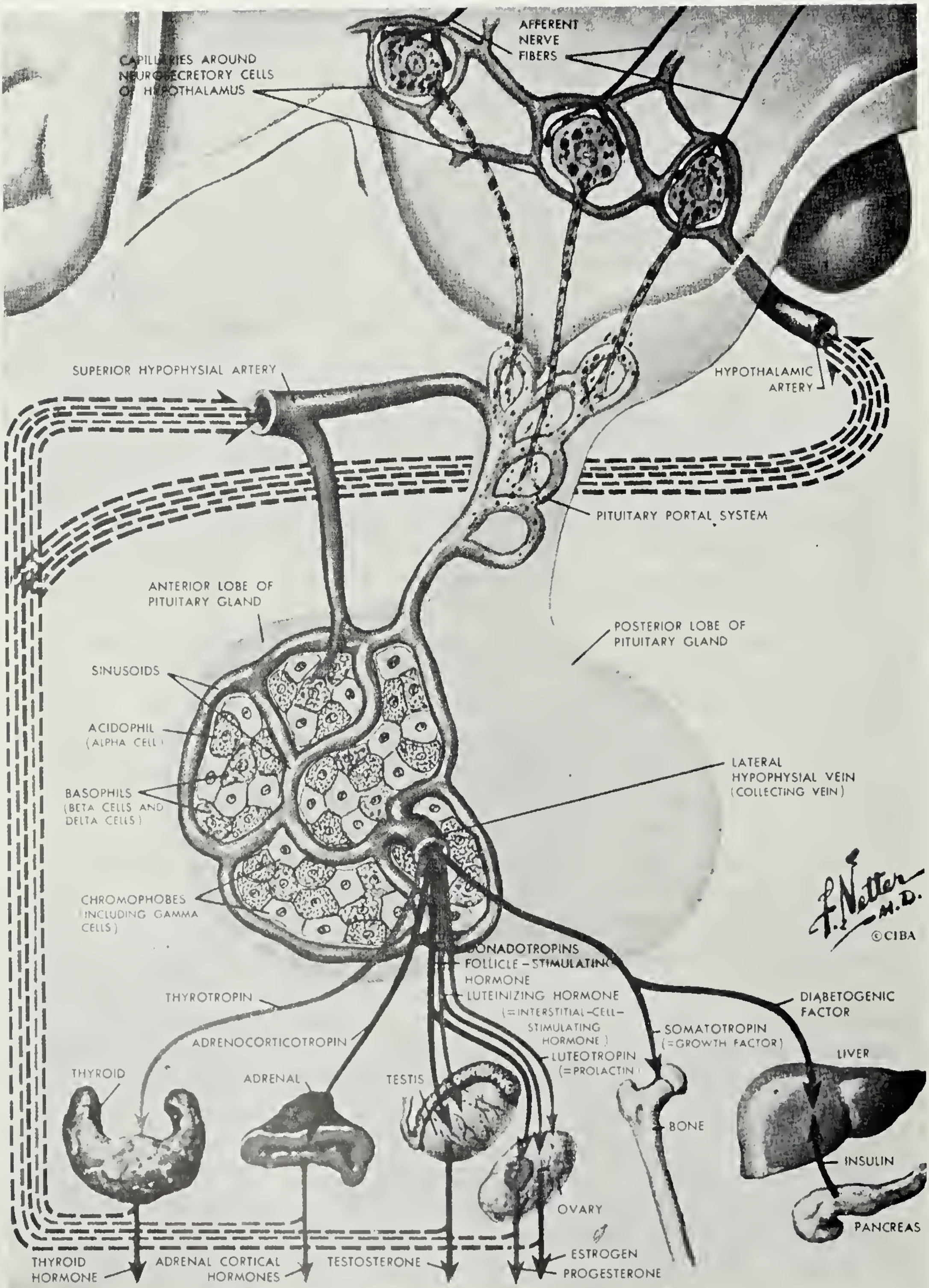


Fig. 47.

Relations of the hypothalamus to the anterior lobe of the pituitary, and the principal secretory activities of the pituitary (from: Frank H. Netter, *The Ciba Collection of Medical Illustrations, Vol. 1, Nervous System*, 1958, p. 155).

ketone level is raised (*ketosis*). Serious disturbance of the pituitary may, obviously, affect the islets and insulin production to the extent, even, of leading to *diabetes mellitus*. These processes clarify the influence of weather, climate and season on diabetes patients (see p. 560).

The functions of the posterior lobe

Crude extracts of the posterior lobe of the pituitary, referred to as *pituitrin*, contain two active substances: *vasopressin*, which causes a slowing of the heart rate, usually a fall in blood pressure (sometimes a slight rise), constriction of the peripheral capillaries and decreasing urinary flow (see pp. 203 and 332), and *oxytocin*, which stimulates contraction of the uterus and is responsible for the onset of parturition.

Higher control of the pituitary

On p. 203 it was pointed out that the posterior lobe, in particular, is stimulated by a dense network of nerve fibres from the anterior nuclei of the hypothalamus. Emotional and other stimuli of the cortex seem, however, to affect the supra-optic and other nuclei of the hypothalamus *via* the thalamus (see p. 206) and are able to stimulate also the anterior lobe, in a neurohumoral way.

Influence of Meteorological and other Environmental Factors on the Hormonal Secretion of the Pituitary

Considering the fact that the hypothalamus is the centre of heat regulation of the human body and registers the changes in environmental temperature and cooling, or heating, and in view of the neural and neurohumoral connections between hypothalamus and hypophysis, it is logical on theoretical grounds to assume that an intimate interrelationship must exist between the meteorological environment and the functioning of the pituitary. This assumption is supported by a considerable amount of evidence collected during the last 50 years both by physiologists and biometeorologists.

The close relationship between weather, diuresis and 17-ketosteroid secretion will be discussed on p. 327. The data to hand indicate a very intimate relationship between weather (*e.g.* influx of cold polar air masses), hypothalamic stimulation and secretion of anti-diuretic hormone by the posterior lobe of the pituitary (being decreased with polar air influxes causing a sudden steep increase in diuresis). Similar influences are known in relation to the hormonal secretion by the anterior lobe of the pituitary.

Growth hormone

The studies of Nylin[1332] and others will be discussed on p. 579, indicating a decrease in bone growth during winter, which suddenly increases in spring and early summer, a process probably related to the differences in ultraviolet radiation and temperature in winter and spring, affecting the calcium metabolism (both the functioning of the parathyroid and vitamin D production, see p. 275), and also showing up in the lower calcium and phosphate level of the blood serum in winter. This problem will be discussed in greater detail on p. 576.

Gonadotrophic hormones

The influence of weather, climate and season on sexual functions, fertility and sex ratio is only partly known, but considerable evidence has been collected indicating a close relationship between these various factors. On p. 203 it was pointed out that stimulation of the nuclei of the tuber cinereum of the hypothalamus affects considerably the sexual behaviour of animals because of the influence of these nuclei on the production and secretion of gonadotrophic hormones by the pituitary. Experimental studies suggest that the cells of these hypothalamic nuclei of the tuber behave like chemical receptors with regard to the gonadotrophic hormones which reach this hypothalamic area. The actual effect of these various processes on the sexual activity depends at least on two factors: (*i*) The concentration of the circulating gonadotrophic hormones; (*ii*) The sensitivity of the cells of the tuber nuclei. The degree of sensitivity depends, at least partly, on the number of cells of these nuclei.

Abnormal sexual behaviour could arise from at least the following three factors: (*i*) Abnormal concentrations of gonadotrophic hormones; (*ii*) Structural (*i.e.* surplus in cells) or functional (*i.e.* strongly increased sensitivity) disturbances of the nuclei of the tuber cinereum; (*iii*) Disturbed interaction of both factors (*i*) and (*ii*).

It is found that the production of gonadotrophic hormones depends on at least four important factors:

(1) *Activity of the CNS.* Ovulation in the rabbit, for instance, takes place within 12–18 hours of coitus, provided the anterior pituitary be not defective.

(2) *Concentration of sex hormones in the blood.* The secretion of gonadotrophic hormones in the pituitary induces the secretion of oestradiol and progesterone (oestrogenic hormones) in the ovary of the female and testosterone (an androgen, *i.e.* a substance with masculinizing properties) in the testis. These various hormones secreted by ovary and testis are known as *sex*

hormones. It is found that if oestrogens or androgens are administered for long periods, considerable enlargement of the anterior lobe of the pituitary ensues. It may cause serious congestion; the functions of the gland are deranged, causing decreased secretion of gonadotrophic hormones, followed by decreased sex hormone secretion. In other words the various components of this complex hormonal system control each other's production.

(3) *Influence of light.* This problem will be discussed more extensively on p. 347, but a few general remarks will be apt here. (*i*) *According to Myerson and Neustadt*[838] ultraviolet radiation applied to the skin of man increases androgen production; (*ii*) *Studies by Fuchs*[1307] *and Hollwich*[1097] seem to suggest a different pituitary function in the *blind*. Their diuresis, carbohydrate metabolism, blood sugar level and reaction to insulin are different from the normal. Apparently, the extent of these discrepancies is proportional to the duration of the person's blindness. The whole pituitary and the surface of the sella turcica (pituitary fossa) seem to be smaller, particularly in persons who have been blind since the age of 6. In a group of blind people nocturnal diuresis was twice that of normal humans and the longer the blindness had obtained, the greater was the nocturnal diuretic frequency. In the same group the reverse situation prevails in daytime, the diuresis being less than that of normal human beings; (*iii*) The evidence of *studies by Benoit and Assenmacher*[1067-1082] since 1933 is that stimulation of the optic nerve by visible sunlight (380–780 mμ) affects the secretion of gonadotrophic hormones, an observation originally made by Bissonette in 1930 (p. 347). The light impulses reach the visual centre of the cerebral cortex which, in its turn, probably stimulates the supra-optic area of the anterior nuclei of the hypothalamus through the thalamus. As a result of neuro-humoral stimulation, the anterior lobe of the pituitary is affected. In ducks it was found that 15 hours of light stimulation per day, at temperatures of 8–15° C, increased the size of the testicles within 2 days. After 3 weeks the volume had increased eighty fold (for further details see p. 347). Benoit also found that direct irradiation of the skull (even after removal of the eyes and eye nerves) with waves > 600 mμ (orange-red and infra-red) stimulates the hypothalamus in various mammals (*e.g.* rats, rabbits and monkeys). It is evident that the seasonal variation in sunlight, in fact even long periods of heavy fog, must affect the functioning of the pituitary and the production of gonadotrophic hormones. (*iv*) *Studies by Milin*[1107-1112] showed permanent changes in the supra-optic and para-ventricular nuclei of the hypothalamus of 30 rats after one month (May) of continuous light stimulation (natural day light during the day and electric light at night). Hypertrophic nuclei and capillary congestion were observed. After 30 days of complete darkness, regressive

structural changes were noticed (for further details see p. 348). Similar observations were made by Pomerat[841].

(4) *Influence of temperature.* The winter period is usually a non-breeding season for animals; the ovaries are quiescent during this period and do not undergo the characteristic cyclic changes. The fact that these animals become reproductively active in winter by prolonged artificial illumination may give the impression that only differences in light intensity affect the reproductive cycle and not the temperature. However, experiments with animals exposed to the cold and normal light conditions have demonstrated a depressive action on the production of FSH and probably also on other sex hormones. Dempsey and Uotila[832] were able to show that nerve stimulation through the pituitary stalk plays an important part in this process. After *transection of the pituitary stalk* the basic rhythm of the reproductive cycle and ovulation, as well as mating, pregnancy and lactation, may remain unaltered, at least in albino rats (studies by Brooks in 1938). Ovulation in the rabbit, however, which normally follows coitus, no longer occurs. In other words, the nerve connections in the stalk are important but not indispensable. Whereas normally the reproductive cycle is lengthened and the ovulation and spermatogenesis are delayed by cold, after transection of the stalk they proceed normally. This suggests that nerve stimulation of the stalk controls the depressive action of cold on the production of gonadotrophic hormones. The same is true for the stimulating effect of cold on thyrotrophin production (see later). This effect disappears after transection of the pituitary stalk. Both observations suggest an intimate relationship between environmental meteorological conditions (in particular changes in temperature and cooling), hypothalamus, pituitary stalk and anterior lobe of the pituitary.

These various data may prove to be of great importance to the study of the *influence of weather and climate on fertility and sexual ratio.* According to Grootenhuis[3183a], there is a striking similarity between the yearly conception-rate curve of horses and the curve of the day length in hours. The possible influence of temperature and air mass on fertility was studied by Müller and Lenz[3187]. Relevant within this context is the fact that a relationship between fertility and the non-protein sulfhydryl concentration of seminal fluid in horses was studied by Werthessen and Haag[3184]. Marden and Werthessen were able to demonstrate an inverse correlation between the non-protein sulphhydryl concentration of seminal fluid of horses and the sperm motility in the seminal fluid. According to Werthessen and Haag, horse fertility is significantly correlated with the sulphydryl concentration, *i.e.* low concentration, high sperm motility and high fertility. Above 20 μg/cc of sulphhydryl in seminal fluid, infertility occurred; with less than 10 μg/cc there was only 55–60% possibility of pregnancy in certain horses (thoroughbred stallion). J. W. Goldzieher[3183] asserts that there is a close relationship between the adrenal cortex and liver function and sulphur metabolism (see p. 653). This selective affinity is shown, for example, by accumulation of sulphur in the adrenal cortex of rats and rabbits following cutaneous applications. As the functioning of the adrenal cortex is greatly affected by changing conditions in environmental temperature and cooling (see p. 279), it is possible that this whole group of meteorotropic phenomena in the pituitary and adrenal gland is responsible for the observed relationship between sexual functions or fertility, and weather, climate and season (p. 265).

Thyrotrophin

It was pointed out that the activity of the thyroid gland is controlled by the hormone thyrotrophin*, which causes the secretion of *thyroxine* by the thyroid gland itself. The production of thyrotrophin is in its turn regulated by the level of thyroxine. If the concentration of the circulating thyroxine is very high, the thyrotrophin production is inhibited (studies by Rawson *et al.*[900]) and the thyroid-stimulating capacity of the anterior pituitary is reduced**. This explains why during hyperthyroidism in animals and man, a consistent decrease of thyrotrophin is observed both in pituitary and body fluids.

The production of thyrotrophin and, therefore, the thyroid-stimulating capacity of the pituitary (also known as *thyrotrophic potency*), varies considerably in different organisms but also in the same animal or person. An excellent summary of the various factors affecting the thyrotrophic potency was given by Adams[856]. They can be classified into biological factors (race and species, age, sex, pregnancy, adrenal gland) and environmental factors (food, and the meteorological influences of temperature, light and atmospheric pressure).

(1) *Influence of race or species.* According to Adams and Allen[857], and other research workers, the thyroid-stimulating capacity of the anterior pituitary in different animals can be classified from high to low as follows: bull-frog, leopard-frog, chicken (old), sole, rat, mouse, dog, pig, sheep,

* Some authors, *e.g.* J. G. Heyland and E. Laqueur (in 1934), believe that there may be two or more thyroid-stimulating hormones, one controlling the changes in weight of the thyroid, one the histological changes.

** See also the studies by Uotila[913] in 1940, which indicate that transection of the pituitary stalk has no effect on these processes. In other words, it is a basic secretory rhythm without the mediation of hypothalamic-hypophyseal nerve pathways.

toad, beef cattle, turkey, man, horse, rabbit, cat, pigeon, chicken (young), guinea-pig, etc. In other words there is *no close relationship between thyrotrophic potency and phylogenetic position of the animal*. However, the anterior pituitaries of some cold-blooded animals (sole, leopard-frog, bull-frog and toad) appear to contain larger quantities of thyrotrophin than those of warm-blooded animals. But within this group of cold-blooded animals, even amongst closely-related forms, there is also a wide divergence in thyroid-stimulating capacity. Some of the disparity, however, may be due to different methods of assay.

(2) *Influence of age*. Thyrotrophic potency increases from pre-puberty to puberty, followed by a decrease, after sexual maturity has been fully established.

(3) *Influence of sex and sexual act*. The male pituitary has been reported to be more potent than the female (at least in rats and cattle). No significant differences seem to exist in human beings. The thyrotrophin content of the pars anterior of rabbits 24–28 hours after mating decreases and is restored 48 hours after coitus (according to Saxton and Greene). Krylow and Sternberg[883] noted rapid and almost complete removal of colloid from the thyroid (see p. 266) in female rabbits just after mating.

(4) *Influence of pregnancy*. According to Bates *et al.*[829], the thyrotrophic potency of cows is greatest in early pregnancy, falling during late pregnancy to the level of the non-pregnant animal. In rats, however, the thyrotrophin content is low during the first half of pregnancy and increases at the end of pregnancy and during lactation. In frogs, in the post-breeding season, there may be twice the amount of thyrotrophin compared with the pre-breeding season. The high thyrotrophic potency seems to be related to high reproductive activity.

(5) *Influence of adrenal gland*. Jores[926] states that adrenalectomy decreases the thyrotrophin content of the rat's pituitary. Injections of adrenaline restored the situation. In normal animals adrenaline slightly raises the thyrotrophin content of the pituitary.

(6) *Influence of food*. Drill *et al.*[872] studied the effect of vitamin deficiencies. Lack of vitamin A leads to increased thyrothrophin production and thyroid activity; vitamin B_1 deficiency, for 6–7 weeks, seems to decrease the thyrothrophin content by 40–50%; vitamin B_2 and vitamin C have little or no effect. Vitamin C seems nevertheless to have some influence, because the thyroid is less stimulated when thyrotrophin is given alone than with vitamin C. Further, a starvation diet for 3 weeks may, but does not always decrease the activity of the thyroid.

(7) *Influence of temperature*. Exposure to cold increases the production of

thyrotrophin and produces intense activity of the thyroid gland. The various cytological changes as a result of this process will be discussed on p. 269. Exposure to heat leads to inactivity of the thyroid. This short-term phenomenon is also observed as a *seasonal* one. In *hibernating* animals like frogs, lizards, turtles, bats, ground squirrels, etc., the thyroid is inactive during winter and active in spring and summer. By contrast, thyroid activity in animals remaining active in winter (sparrow, albino rats, etc.) is higher in winter and lower in summer.

According to studies by Riddle and Fisher[901] in 1925, using 3 species of pigeons kept on the same diet throughout the year, in early spring with increased thyrotrophin production and thyroid activity there is an excess of male offspring, whereas, during periods of less activity and smaller sized thyroid (in summer), there is an excess of female pigeons. Similar observations on *changing sex ratios* through the year were made previously by Adler[858] in frogs (around 1917) and by Whitman in 1919. Riddle[901] explained these changes as the resnlt of progressive diminution of metabolism within the ova (see later). As these changes in thyrotrophin production are mainly due to seasonal changes of meteorological conditions, the various reports by Petersen[17] and others on changing sex ratios in different periods of the year may prove to be correct.

Studies by Uotila[911] in 1939 have shown that after transection of the pituitary stalk, cold stress does not create an increased thyrotrophin secretion. Put differently: the *hypothalamic-hypophyseal nerve pathways are able to transmit impulses in case of emergency as a result of exposure to a cold environment.* On the other hand, hypophysectomy is followed by thyroid atrophy, even if the thyroid sympathetic stimulation continues. During cold stress in these conditions the body temperature falls rapidly. Therefore, normal functioning of both the pituitary and the pituitary stalk is required to create the increased thyroid reaction after cold stress. Lebond *et al.*[885, 886] showed that the cold stress phenomena gradually disappear (at least in rats) if the stress condition continues for a long period. A kind of accommodat on (see p. 241) takes place. Rats exposed to −2 C exhibit a pronounced increase in thyrotrophin production (increased functioning of the thyroid) after 7 days, which reaches a maximum after 26 days. At the end of 40 days' exposure the thyrotrophin production reverts to normal. This would suggest that during winter a cold stress created by a cold front or influx of polar air masses is *less effective in increasing thyroid activity than in summer.*

(8) *Influence of light.* The evidence of studies by Higgins *et al.*[921] suggests that, at least in chickens, shortage of ultraviolet light or vitamin D defi-

ciency may cause four pronounced physiological changes, *viz.*, the cortex becomes less compact; the parathyroid increases in size, often attaining weights 8 or 10 times the normal value; the thyroid becomes hyperplastic; the bones are soft. After increased U.V. radiation the bones become firm and hard, the calcium content of the blood (regulated by the parathyroid, see p. 275) is restored (from 6.8–11.5 mg/100 cc); the same is true for the phosphate content of the serum (rising from 3.9–4.6 mg in 100 cc); the parathyroid becomes normal in size; the same is true for the thyroid. The studies made by Benoit, Assenmacher and Milin (see p. 347), using visible light, also support the assumption that changes in intensity and spectrum of sunlight in the course of the year seriously affect the functioning of the pituitary, thyroid and parathyroid. But an exceptionally sunny summer and autumn, such as enjoyed from June to September in 1959 in Western Europe (with 1038 hours of sunshine in the Netherlands against 764 normal) or the difference in spectrum and intensity, particularly of U.V. radiation, at great altitudes, must have its specific bioclimatological effects, in the latter case particularly if a person is transferred abruptly from low lying land to high altitudes. In the next section, on the thyroid gland, these various problems will be discussed in more detail.

(9) *Influence of atmospheric pressure.* According to Gordon *et al.*[877], rats subjected to low atmospheric pressures (280–250 mm Hg) for 6 hours or 18 to 20 hours daily, for 14 to 20 days, have less thyrotrophin in their serum. The pituitary content remains normal. The thyroid, however, is less active; similar observations were made by Verzár *et al.*[916] in Switzerland. Their experiments will be discussed in the following section on the thyroid.

2. *The Thyroid Gland*

General anatomy

The importance of the thyroid gland, particularly where bioclimatological phenomena are concerned, was stressed repeatedly in the previous section. The gland is located in the neck near the junction of larynx and trachea. It is composed of two connected lobes, one on each side of the trachea, and consists of aggregations of spherical or oval vesicles (known as *follicles* or *alveoli*), lined by granular cubical cells. The cavities of the vesicles are filled with a homogeneous viscid iodine-containing substance, known as the *colloid*, which is secreted by the epithelial lining. The colloid is lacking in the new-born infant, the whole gland consisting of solid masses of epithelial cells.

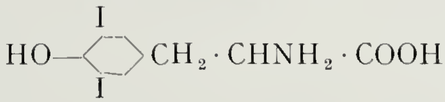
The normal human thyroid weighs from 25 to 40 mg, but varies considerably in size with age, reproductive state, diet, etc. The vascular supply is exceptionally rich. In proportion to its size, more blood flows through this gland than through any organ of the body, with the possible exception of the adrenal gland.

Regulation of thyroid secretion

We have seen that the function of the thyroid depends on an active principle called *thyroxine*. The regulation of this thyroid secretion is controlled by two mechanisms:

(1) The gland is stimulated by post-ganglionic fibres of *nerves from the middle cervical ganglion of the orthosympathetic nervous system*. However, it is found that secretion of thyroxine may continue normally after these nerves have been destroyed.

(2) The principal regulator is the *anterior lobe of the pituitary* (see p. 257) by means of the hormone thyrotrophin, which produces thyroxine secretion and regulates the uptake of iodine, which increases with increased thyrotrophin production. The thyroid contains 20% of the total iodine content of the body. We stated on p. 263 that thyrotrophin and thyroxine production form a self-regulating system. Hypophysectomy leads to atrophy of the gland and reduced uptake of inorganic iodine from the plasma. The iodine is absorbed from the food in the small intestine and brought into the blood plasma and thyroid gland. It is taken up in inorganic form but gradually built up into complex organic compounds. In the gland iodine is mainly present in three forms: *inorganic iodine* (10%), *diiodotyrosine*



and related compounds (75%) and *thyroxine* (15%)*. The last named is stored in the gland with a protein known as *thyroglobulin*. After a few hours diiodotyrosine disintegrates, the thyroxine content increases and organic iodine gradually appears in the serum as thyroxine, probably combined with serum albumin. The average iodine content of the blood serum in summer amounts to about 13γ/100 cc (according to Kendall[881]). Veil and Sturm[914] stated that in late summer and autumn the iodine content is 12.8γ/100 cc, in winter it is only 8.35γ/100 cc (according to Maurer[889], 9.25γ). The iodine content varies considerably in women. On the first day of menstruation it may increase by more than 100% (*e.g.*, from 9.3–19.3 γ). Also during pregnancy, shortly before confinement, the iodine content is usually more than 100% above normal, followed by a sudden decrease to below normal after birth.

* Thyroxine can be defined chemically as the *p*-hydroxyphenyl ether of the amino acid tyrosine with four iodine atoms.

Physiological effects of thyroxine

Thyroxine stimulates general metabolism, it mobilizes glycogen from the liver, it accelerates the heart, it may cause the removal of calcium (together with phosphate) from the bones and influences renal secretion (probably not directly but through its influence on metabolic processes in general). Thyroidectomy reduces urinary flow in diabetes insipidus (see p. 333); in normal subjects thyroid extracts have a diuretic action. According to Ellinger (see p. 567) thyroid activity is related to sensibility of the skin to U.V. light, which could explain the seasonal fluctuations in complaints of patients suffering from exophthalmic goitre (see later p. 561). Studies by Fischer and Griffin (see p. 294) suggest the influence of thyroid activity on taste-threshold.

(1) *Thyroid deficiency (hypothyroidism)*, due to shortage of thyroxine, may lead to *myxoedema* a condition characterized by swelling of hands and face, slow pulse, dryness and wrinkling of the skin, falling out of hair, diminution of mental activity, loss of memory, slowness of thought and speech, sluggishness of movement, pains in muscles and joints, disturbed sexual functions and abnormally low basal metabolic rate (30–40% below normal), causing an increase in body weight. Usually the cholesterol and total protein level of the serum are increased. Often a depressed activity of the bone marrow is observed, causing anaemia. In this connection the following observations are highly significant. It transpired from studies by Goldberg[1201] in 1938 and Levin and Leathem[1202] in 1942 that hypophysectomy in dogs, rats and monkeys produces a fall in serum albumin and an increase in serum globulin. Administration of desiccated thyroid caused a return of the globulin towards the normal level, but had very little effect on the serum albumin. However, adrenocortical extracts prevent the drop in serum albumin, without affecting the increase in globulin level. Stilbestrol, a potent stimulant to the adrenal cortex does the same. According to Piliero and Pansky, adrenalectomy in rats results in significant decreases in the albumin level. These and other experiments suggest that the *serum globulin level is controlled by the thyroid gland, the albumin level by the adrenal cortex.*

A special form of myxoedema, existing before birth (congenital myxoedema), is known as *cretinism* in children.

A third form of hypothyroidism, but due to iodine deficiency (*e.g.* due to iodine shortage in food or water), is *thyroid hyperplasia* (*i.e.* abnormal increase of tissue elements resulting in increase in size) which may lead to simple goitre or *struma*. According to Sturm similar hyperplastic phenomena of the thyroid are observed during pregnancy and the menstrual cycle. Various experiments suggest that oversecretion of thyrotrophin, combined with a deficiency in circulating thyroxine, is actually responsible for this iodine deficiency. Certain sulphur containing compounds, like thiouracil $CS(NH_2)_2$, also, induce thyroid hyperplasia by inhibiting the enzymatic processes required for thyroxine synthesis.

(2) *Excessive activity of the thyroid gland (hyperthyroidism)*, due to increased production of thyrotrophin, leads to an actual enlargement (hypertrophy) of thyroid tissue, resembling thyroid hyperplasia. The cytological changes will be discussed in greater detail below. Various stress conditions, either affecting the cortex or the hypothalamic anterior pituitary system, may lead to excessive thyroxine secretion and hyperthyroidism. During a state of hyperthyroidism the oxygen consumption and general metabolism increase considerably. The same holds for CO_2 production and nitrogen secretion. The body weight decreases. According to Oswald[897], all these phenomena are particularly prominent in persons having a rather *unstable, readily over-stimulated, nervous system*. In these circumstances loss in body weight can be very considerable (20 kg in 14 days), whereas other persons on the same diet remain constant in weight. In this nervous group of people iodine treatment or X-ray treatment may cause hyperthyroidism, which is lacking in the control group. This observation of Oswald's is very important and may account for the different degree of meteorotropic effects noted in the thyroid of different people under the same meteorological stress conditions.

A serious form of hyperthyroidism is known as *Grave's disease* (*exophthalmic goitre* or *morbus Basedowii*). It is characterized by increase in basal metabolic rate up to 50%. The increased evolution of heat is compensated by dilatation of the cutaneous arterioles and capillaries (see p. 214). Also, a considerable increase in heart rate (up to 140/min) and excitability of the heart muscle are observed; the bloodsugar level may rise, causing *glycosuria;* serum calcium tends to fall; frequently there is depressed liver function. A retraction of the upper eyelids (staring) and exophthalmos (abnormal protrusion of the eyes) are common.

Influence of meteorological factors

Apart from the influence of food and water (affecting the iodine content), a very important environmental factor affecting thyroid function is the meteorological environment, in particular the influence of temperature (and cooling), sunlight and atmospheric pressure.

(1) *Influence of temperature.* Many studies have been made on the influence of cold and heat stress on thyroid function, *e.g.* by Cramer and

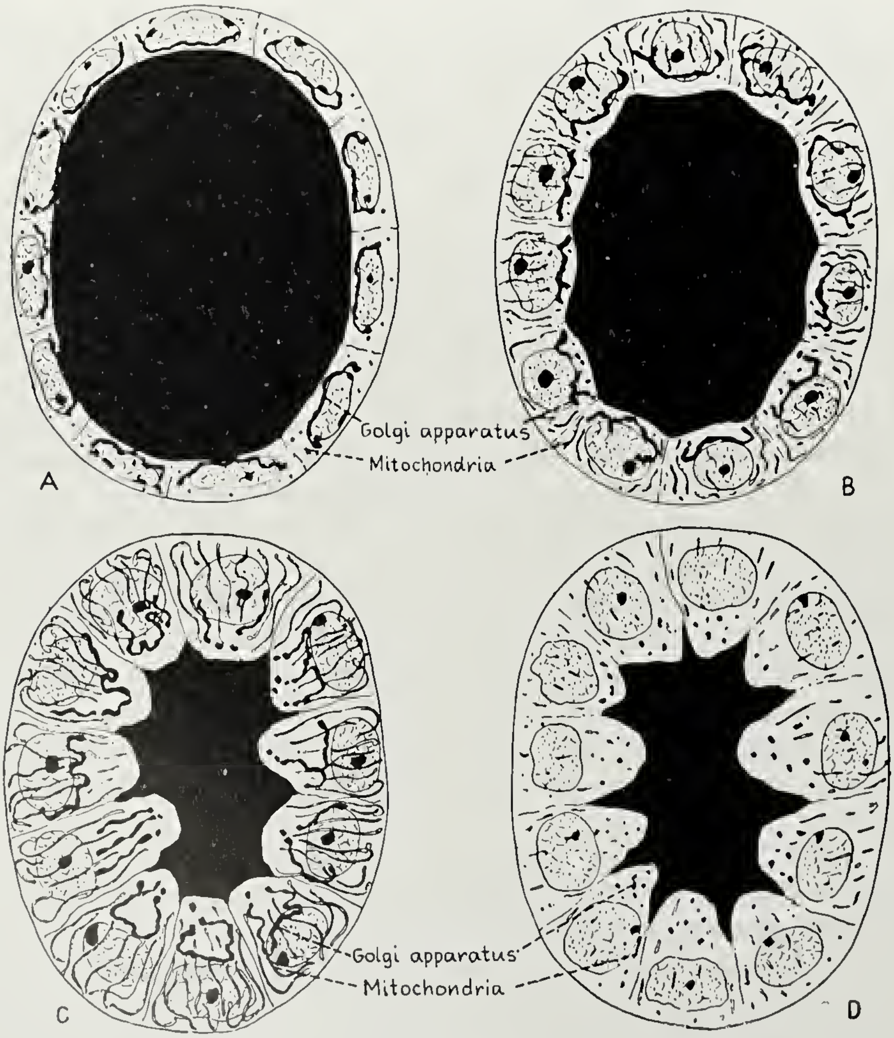


Fig. 48.
Influence of heat and cold stress on the thyroid gland (after Cramer and Ludford[869]). A: Resting; thyroid fed; exposure to heat; B: Moderate degree of activity; fasting; C: Extreme degree of activity; exposure to cold; action of β-tetrahydronaphthylamin; D: After extreme degree of activity; following exposure to cold or action of β-tetrahydronaphthylamin.

Ludford[869], Baillif[861], Uotila[910–913] and many others[856–920]. When discussing the influence of temperature on the functioning of the pituitary (see p. 262) we briefly mentioned the effect of the thyroid. It was pointed out that transection of the pituitary stalk or complete hypophysectomy prevents the cytological changes observed in the thyroid after temperature stress. During rest, the cells of the thyroid gland, unlike most gland cells, do not

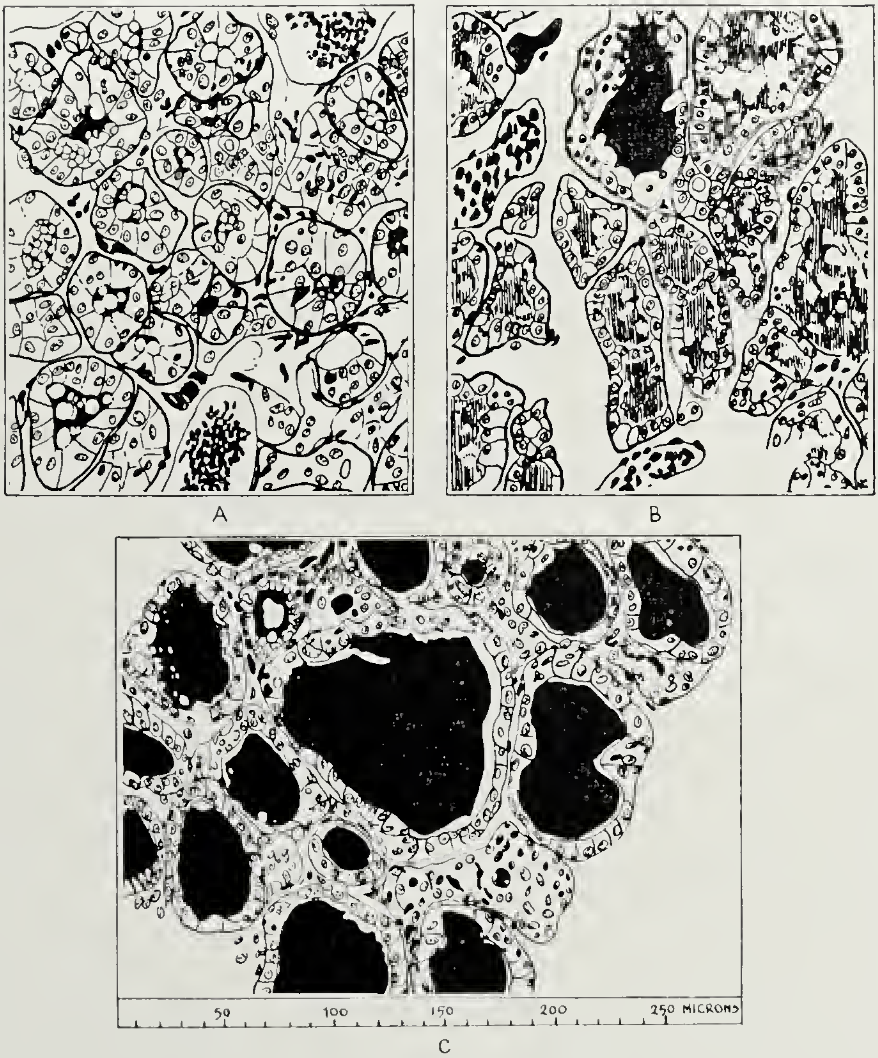


Fig. 49.
Influence of cold (following heat) and heat (following cold) on the thyroid of mouse (magnification 300 x) (after Cramer and Ludford[869]). A: the thyroid was kept at ordinary room temperature; B: mice were kept in glass jars placed in an incubator at 37°C at 10 a.m. and removed at 5 p.m. From 5 p.m. till 5 a.m. they were kept in a room with open window during cool weather in March (immediate effect of cold, following heat); C: after this routine took place several days, the mice, after being back in the warm incubator for 6 hours, were killed and the thyroid was studied (immediate effect of heat, following cold).

contain their specific secretory product within themselves to any great extent. Therefore, changes in the cells are not due to mechanical reasons, such as accumulation and subsequent rapid discharge.

Effect of cold stress (see Fig. 48, lower part, and Fig. 49B). Cold produces intense activity of the gland. The activity manifests itself by intense congestion of the intra-alveolar capillaries and by disappearance of the colloid from the alveoli. The congestion of intra-alveolar capillaries may be so intense that haemorrhages into the centre of the alveoli may occur. Cells lining the alveoli may get detached and pushed into the central lumen of the alveoli.

Effect of heat stress (see Fig. 48, upper part, and Fig. 49C). Warmth induces inactivity of the gland (according to Mills[893] the same phenomenon is observed after injection of quinine or morphine sulphate). The colloid accumulates in the alveoli. Inter-alveolar capillaries close up altogether, so that the lining cells appear to be resting directly upon the basement membrane. The influence of temperature on cytological changes is demonstrated in Figs. 48 and 49. Cramer and Ludford[869] observed that, with increased thyroid activity, the mitochondria* of the cells become more and more differentiated from the cytoplasm, they enlarge and become filamentous, while with diminishing activity their differentiation from the cytoplasm becomes less distinct, only few granules remaining visible. After prolonged increased activity of the gland the large threadlike forms break up into shorter rods. The Golgi apparatus has a simple contracted form in the resting cell; during activity it enlarges, becomes convoluted and finally breaks up. During intense secretory activity the chromatin content also decreases. In other words, temperature stress affects the mitochondrial apparatus of the cytoplasm. It changes the surface of the mitochondria; it either increases during activity or reduces during rest. Similar processes have been observed in the adrenal medulla and liver.

As substances with lower surface tension tend to accumulate at the surface, during thyroid activity the increased inner surface (and surface tension) will favour the accumulation of lipoids around the mitochondria. When thyroid activity decreases and the inner surface diminishes, the lipoids return to the cytoplasm. This ebb and flow of lipoids must affect the concentration of lipoids in the cytoplasm and cell membranes. During great activity of the thyroid (cold stress) the lipoids will be drawn from the membranes and, as a result, the *membrane permeability* decreases (see p. 335).

(2) *Influence of light.* The influence of light on the pituitary and, indirectly, on the thyroid, were discussed on p. 261. Higgins *et al.*[921], Bergfeld[864], Puntriano and Meites[898], Turner and Benedict[909], Dempsy[870] and many

* Mitochondria are round or rod-shaped bodies composed of optically positive uniaxial, micellae crystals. They resemble Lehman's fluid crystals with their winding movements. Their function is unknown, but they seem to influence the oxidation processes in the cells and may be the actual cause of secretion of gland cells.

others observed hyperplasia and colloid loss in the thyroids of animals as a result of ultraviolet deficiency or complete darkness. This is accompanied by high iodine content of the thyroid, but low iodine blood serum level; increase of ultraviolet radiation or continuous light causes the opposite effect. In other words there is a struma-like degeneration. Bergfield[864] showed in greater detail that ultraviolet-C (wavelength less than 300 mμ), more specifically, has this hyperplastic effect. Light waves of 290–320 mμ (ultraviolet-B) have an opposite effect. Due to photochemical action, the latter rays convert an inactive sterol in the skin, *7-dehydrocholesterol*, into the anti-rachitic substance vitamin D_3. This explains why it was that the size of thyroids of rats kept in complete darkness could be reduced, not only by direct radiation, but by feading the animals with extracts of radiated skin. Bennholt-Thomsen and Wellman[863] were able to confirm these results. On p. 576 the yearly changes in iodine content of the blood and other organs will be discussed in more detail.

The combined effect of low temperatures and ultraviolet deficiency in winter was demonstrated by Riddle and Fisher[901] in 1925, using 3 species of pigeons kept on the same diet throughout the year. This 3-year experiment revealed the following: (*i*) There was a simultaneous enlargement of the thyroid in all three species in autumn and winter and a progressive decrease during spring and summer. The changes occurred independently of diet, care, locality, race, age, length of confinement, body size, etc; (*ii*) The period when the size of the thyroid declines in pigeons is the season of active reproduction; (*iii*) As stated on p. 265, predominance of male offspring coincides with periods of larger thyroid size (early spring), while that of females is noted when the thyroid is smaller (summer). It was found that the early spring male-producing eggs are smaller than the female producing summer eggs. According to Riddle, the male eggs have a higher metabolic rate, oxidize more of the injected material and store less of it, whereas the larger female eggs of late summer have a lower metabolic level and oxidize less. Riddle observed not only a difference in sex ratio but also a difference in body structure of many female pigeons born in early spring. They were more masculine than those born in late summer. The most feminine females (as shown by copulatory behaviour, etc.) are born in late summer.

(3) *Influence of atmospheric pressure.* The decreased thyroid activity at very low atmospheric pressures was mentioned on p. 266. Verzár[916] (Physiological Department of the University of Basel), Sailer (High Altitude Research Station, Jungfrau Joch) and Vidovič (Climatic Physiological Station, St. Moritz) studied the activity of the thyroid gland in 144 rats by measuring the uptake of ^{131}I over a period of several days. The rats were brought from

Basel (altitude 280 m, 732 mm Hg) in 8 hours to 3450 m (490 mm Hg). Reduction of atmospheric pressure to 250 and 380 mm Hg retards the ^{131}I uptake. The lower the pressure, the less concentrated is the iodine in the thyroid. At 490 mm Hg (= 3450 m altitude) a small decrease in activity can be seen, but not at 2010 m (592 mm Hg). The depression of the thyroid is only temporary; after a few days it becomes normal again. Below 480 mm body temperature also decreases, but this is restored to normal in 3–4 days. As considerable reduction in heat production takes place upon removal of the thyroid, the fall in temperature seems to be due, at least partly, to decreased thyroid function. However, certain ^{131}I experiments have shown that the thyroid was already normal, yet body temperature was low. Verzár *et al.* believe that the low partial oxygen pressure causes and *increased adreno-cortical activity,* which may be interconnected with the decreased thyroid activity. This assumption is supported by the following observations: (*i*) Evans[874] was able to demonstrate adrenal cortex hypertrophy at very reduced partial pressure of oxygen; (*ii*) The same was observed by Sundström and Michaels[2197] in 1942, at pressures below 350 mm Hg. At higher pressures there was neither fall in body temperature nor hypertrophy of the adrenal cortex; (*iii*) Verzár and Vidovič[915] found in 1951 that injections of adrenocortical hormones can inhibit thyroid activity.

These three facts seem to support Verzár's point that liberation of ACTH at very reduced atmospheric pressure or during oxygen lack and consequent secretion of AC-hormones are responsible for decreased thyroid activity.

3. *The Parathyroid Gland*

General anatomy

Another important gland associated with biometeorological phenomena is the parathyroid. The parathyroid glands are very small (7 mm long and 3–4 mm wide), flattened, ovate or pyriform bodies situated on the posterior surfaces of the lateral lobes of the thyroid. In men there are usually four parathyroid glands, a superior and an inferior pair. The blood supply is chiefly from the inferior thyroid arteries. The glands consist of masses and cords of epithelial cells between which numerous small blood vessels are interspersed.

The active principle of the gland is the *parathyroid hormone,* also known as *parathormone.*

Physiological effects of parathormone

The physiological effects of parathormone are the following:

(1) *Control of the calcium level of the blood.* Removal of the parathyroid

causes a fall in serum calcium from 9–12 mg/100 cc (in normal subjects) to 8 or 6 mg. A surplus of parathormone may cause a rise in calcium level to 15 mg %. It is accompanied by loss of appetite, drowsiness, etc.; the blood becomes viscid, the blood volume decreases, urea concentration of the blood rises, and so on. Most of the calcium present in the body is stored in the osseous system as a calcium phosphate-carbonate compound. In the normal organism calcium is deposited and absorbed from the bones continuously. Only small amounts are present in the blood plasma, mainly as diffusible calcium ions or non-diffusible calcium proteinate. Calcium is absorbed from calcium containing foods (milk, cheese, green vegetables, cereals) in the upper portion of the small intestine, an area which remains acid on account of gastric juices. About 70% of injected calcium is excreted in the faeces. The amount of calcium which is absorbed depends on a number of factors: it increases with increased *acidity* of the intestine [alkaline bowel gives insoluble $Ca_3(PO_4)_2$ and $CaCO_3$] and particularly with increased vitamin D content (which is influenced by ultraviolet radiation, see p. 341); incompletely absorbed fats form with calcium in the intestine insoluble soaps leading to calcium loss; high phosphate intake causes calcium loss due to formation of insoluble $Ca_3(PO_4)_2$; phytic acid (inositol hexaphosphoric acid ester) in cereals precipitates calcium as calcium phytate;

The main functions of the calcium in the body are the following:

(α) It is essential for *ossification of bones and teeth* (vitamin D deficiency may cause rickets).

(β) It regulates the *excitability of nerve fibres and nerve centres.* Removal of the parathyroid glands causes tetany, characterized by hyperexcitability of peripheral nerves, and motor nerves, particularly in young animals. A diet rich in meat produces a similar effect. It is accompanied by intermittent contractions (spasms) of the muscle system and may lead to stiffness in the legs, violent fits, etc.

(γ) It is required for *contraction of the heart muscle.* Increase in Ca ions in the blood increases the force of the heartbeat. In the presence of an excess the heart contracts well, but relaxes insufficiently.

(δ) It is necessary for blood clotting (see p. 318), because coagulation as a result of the interaction of thrombin and fibrinogen (forming insoluble fibrin) depends on the formation of thrombin from prothrombin in the presence of free calcium ions and other substances.

These facts clearly indicate that environmental factors affecting the functioning of the parathyroid and calcium metabolism are able to disturb various important physiological processes in the body.

(2) The calcium level is closely related to the *phosphate level,* which occurs as inorganic phosphate in cells or in organic compounds in nervous tissues and muscles. The phosphate absorption in the intestine is also greatly affected by the vitamin D level. In the blood serum the quantities of Ca and PO_4 are in inverse ratio. An increase of the one causes a decrease of the other. The

normal PO_4 serum level is 3–5 mg/100 cc. The seasonal changes will be discussed on p. 576.

(3) *Possible control of the magnesium level of the blood*[1261–1269]. It is known that in cattle a typical seasonal disease occurs, known as *grass tetany,* as a result of magnesium deficiency. In man the normal amount is about 2.1–2.8 mg/100 cc. Magnesium deficiency decreases the solubility of calcium salts in the blood, it causes hyperexcitability of the nerves, vascular disturbances and so forth. These effects are intensified if the diet is rich in calcium (according to Tufts and Greenberg, in 1938). Experiments by Greenberg and Mackay in 1932 suggest that injection of parathyroid hormones increases the magnesium serum level. Bulger and Gausmann (in 1933) were unable to confirm this observation. On the other hand, according to Bassett (in 1935), parathyroid removal causes a temporary fall in magnesium secretion. Agna and Goldsmith (1958) state that hyperparathyroidism may create *hypomagnesaemia,* characterized by hyper neuro-muscular excitability, even if the calcium level is normal. In view of these observations several physiologists are inclined to believe that the parathyroid plays an important part in controlling the magnesium balance of the body.

Control of parathyroid secretion

The secretion is probably regulated by the calcium concentration of the blood reaching it. If the blood serum becomes supersaturated with calcium, some is precipitated in the bones. In parathyroid deficiency less calcium is present in the serum. During hyperparathyroidism, calcium flow from the bones produces *hypercalcaemia* and decreases the phosphate level of the blood *(hypophosphataemia),* which may lead to the disease known as *osteitis fibrosa.*

Influence of meteorological factors

(1) *Influence of temperature.* (*i*) Cold stress seems to create a parathyroid deficiency and fall in calcium level of the blood serum. (*ii*) According to Allcroft[1261, 1262], in cows the magnesium level is low (and grass-tetany is common) if meteorological conditions during the preceding period have caused a strong cooling effect. As a result, low magnesium values are found more specifically in those periods when the mean minimum temperature is lowest for the year, but also in all periods when temperature falls below 5.5° C and sunshine is scarce, rainfall preceding the period is high and of frequent distribution, winds are strong and frequent, precipitation is accompanied by hail or snow. In other words, many periods preceded by

active cold fronts and the influx of cold polar air are particularly favourable to the creation of magnesium deficiency and its clinical consequences. (*iii*) Folk[1298-4300] was able to demonstrate a high magnesium level in *hibernating* animals, like bats, as soon as the oesophageal temperature had dropped to 13° C. Similar observations were made by other investigators in other hibernating animals. The various thermal effects on parathyroid function suggest that the parathyroid is affected in a neurohumoral way by the hypothalamus and pituitary.

(2) *Influence of light.* As indicated on p. 273, a shortage of U.V. light may cause the parathyroids to increase considerably in size, at least in chickens.

4. The Adrenal Gland

General anatomy

One of the most important glands, after the pituitary, from a meteorotropic point of view, is the adrenal. It consists of two flattened, rather crescentic, bodies located in the retroperitoneal tissue along the cranial ends of the kidneys. The two glands of a normal adult weigh about 12 grams. They receive blood through numerous small arteries arising from the adrenolumbar arteries, the aorta and the renal arteries. The glands consist of two parts with different functions, the *cortex* and *medulla*, the cortex being yellowish because of abundant lipoid, the medulla reddish-brown due to the presence of much blood. The cortex consists of columns of polyhedral cells with well marked nuclei and numerous lipoid granules in the cytoplasm, whereas the medulla is composed of irregularly arranged cells which show a dark staining with chromic acid because of the presence of the hormone *epinephrine* (better known as *adrenaline*), $C_9H_{13}NO_3$, which is present in the medulla in relatively high concentrations.

Physiological properties of adrenal gland

(1) *Active principle and control of adrenal medulla.* Through its active principle adrenaline, the medulla is functionally closely related to the orthosympathetic nervous system (see p. 191). It is not definitely known whether the medulla also discharges adrenaline in rest, but it is certain that in various states of emergency and stress adrenaline is poured into the circulating blood and therefore reinforces the stimuli created by the orthosympathetic nervous system. The influence of adrenaline on various physiological functions in the body was summarized on p. 192. Adrenaline seems to act only peripherally. It does not act on the anatomical sympathetic nerve endings. The *nervous control* of the medulla takes place by means of

preganglionic splanchnic nerve fibres which end directly round the medullary cells themselves. The chemical transmitter between these preganglionic fibres and adrenal cells is acetylcholine (see p. 192). It is found that adrenaline secretion is stimulated by a number of factors, both environmental and endogenous: physical and emotional stress; cold stress; oxygen stress due to shortage of oxygen as a result of high altitude (anoxia) or inhalation of poisonous gases (carbon monoxide, coal gas etc. causing asphyxia); fall of arterial blood pressure; anaesthesia; hypoglycaemia (*i.e.* fall of the blood sugar below the normal level of 80-120 mg/100 cc, *e.g.* due to dysfunction of the islets of Langerhans, see p. 257, causing hyperinsulinism, etc.).

(2) *Active principle and control of adrenal cortex.* Extirpation experiments have shown that the cortex is essential to life, but the medulla is not. *Dysfunction* of the adrenal cortex may cause loss in weight, disturbances in *ionic balance* of the blood (*e.g.* NaCl in plasma is decreased probably due to increased excretion, potassium increased), disturbed *water balance* (leading to accumulation of excess fluid in the tissue cells, decreased glomerular filtration of the kidney and decreased flow of urine), the general *metabolism* is depressed, the absorption of carbohydrates from the small intestines is slowed down, deposition of glycogen in the liver is depressed, there is a tendency to hypoglycaemia, *capillary resistance* is decreased (permeability increased), the *plasma volume* decreases (causing increased red cell count and haemogobinl concentration), rise in *plasma protein concentration,* fall in albumin level (see p. 268). In very serious cases these processes may lead to *Addison's disease* (see p. 255). The active principle causing these physiological changes seems to be due to certain substances in the adrenal cortex which all belong to a very complex group of organic coumpounds, the *sterols*. They are often divided into three groups; the *benzene-soluble crystalline sterols* (17-ketosteroids) to which belong corticosterone, 11-dehydrocorticosterone, desoxycorticosterone, progesterone and various androgens and oestrogens (see p. 524); *water-soluble crystalline sterols* (*e.g.* 17-hydroxy-11-dehydrocorticosterone) and an *amorphous fraction* (responsible for 90% of the total potency of adrenal cortex extracts), this latter fraction being particularly responsible for the ionic balance. One of the most potent hor- mones of the adrenal cortex is *aldosterone* (about 20 times more potent than desoxycorticosterone) which plays an important role in sodium and potas- sium secretion and retention (see p. 320).

Influence of internal factors

(1) *Influence of the pituitary.* On p. 257 it was pointed out that the activity of the adrenal gland is controlled by adrenotrophin, a hormone secreted

by the anterior lobe of the pituitary. Hypophysectomy causes an atrophy of the adrenal cortex, which can be eliminated by injecting ACTH. Disturbances in pituitary function will be reflected in the function of the adrenal cortex and this may explain why environmental changes in meteorological conditions may effect the adrenal gland through the hypothalamic-pituitary tract.

(2) *Influence of vitamin C.* Dugal and Thérien[615] demonstrated that the hypertrophy of the adrenal gland, observed during cold stress, is inhibited if vit. C is given to the animal in large quantities. Studies by a number of authors (Sayers *et al.*) have shown that with increased activity of the gland ascorbic acid and cholesterol level of the gland decreases. This decrease the takes place more quickly (according to Dugal) when the animal is exposed to cold. Studies by Leblanc[691, 692] confirmed these observations. The influence of vitamin C is noticeable within 24 hours. Application of vitamin C decreases the cholesterol level of the adrenal gland. In other words, it increases the activity of that gland. Small concentrations of ACTH with vit. C are able to prevent atrophy of the adrenal cortex after hypophysectomy, which ACTH alone in these concentrations could not produce.

(3) *Influence of adrenal gland on thyroid.* Various observations suggest the influence of the adrenal gland on thyroid function: (*i*) As indicated on p. 264, adrenalectomy decreases the thyrotrophin content of the pituitary. Injection of adrenaline can restore the situation. (*ii*) Verzár and Vidovič[915] observed that injections of adrenocortical hormones can inhibit thyroid activity (see p. 274). The release from and the concentration of the radioisotope ^{131}I in the thyroid of rats is diminished by adrenal cortex extracts. It is not known whether this directly affects the thyroid or indirectly through the pituitary, which is brought to secrete less thyrotrophin. After adrenalectomy the iodine concentration is usually higher than normal. On the other hand, changes in thyroid function are reflected in the adrenal. For example, hyperthyroidism (after cold stress) causes hypertrophy of the adrenal cortex; hypothyroidism causes atrophy of the cortex.

Influence of meteorological factors

(1) *Influence of cold fronts and polar air masses.* As indicated above, cold stress creates hyperthyroidism and hypertrophy of the adrenal cortex. The meteorotropic effects have been studied extensively in relation to 17-ketosteroid secretion and capillary resistance (or permeability). These observations will be discussed in a later section more extensively, but a few preliminary remarks will be made at present.

The influence of weather on *17-ketosteroid secretion* was studied for the first time by Zimmerman[1304, 1306] during a relatively short period. The present author repeated these studies on a larger scale for a period of $1^1/_2$ years. Daily 17-ketosteroid analyses of urine of a healthy male clearly demonstrated a sharp rise each time an active cold front or cold polar air reached the city of Leyden (the Netherlands). The greater the temperature contrast with the preceding period, the greater the increase. A steep fall was observed during warm air influxes. In winter the general 17-ketosteroid secretion is higher than in summer (see further p. 328).

The influence on *capillary resistance* (*i.e.* the capacity of the capillary wall to resist intracapillary pressure or extracapillary suction) was studied by Robson and Duthie in Great Britain, Eichholtz *et al.* in Germany and Kramár *et al.*[510, 511] in the U.S.A. They assume that the adrenal cortex and pituitary are intimately connected with the control of capillary resistance. Both corticosteroids and the growth hormone seem to be involved in this process. Corticosteroids and adrenaline increase the resistance, whereas growth hormone, pilocarpine (see p. 335) and histamine have a decreasing effect. The actual mechanisms involved will be discussed on p. 555 (Enzyme activity in rheumatic diseases). In other words, the capillary resistance* reflects the balance between two antagonizing groups of hormones. According to studies by Regli and Stämpfli in Switzerland[1378] and Arimatsu[1377] in Japan, capillary resistance increases after cold front passages and decreases after warm fronts. Similar meteorotropic phenomena were observed in 1955 by Lotmar (Rheumatism Clinic of the University of Zurich) and Häfelin (Swiss Central Meteorological Service) in Switzerland[1376], using radioactive sodium sulphate solutions injected in the ear veins of 21 rabbits. The experiments were carried out for 188 consecutive days. On days when cold fronts were passing, the skin permeability of rabbits proved to be low, whereas on warm front or foehn days high permeability was observed.

(2) *Influence of atmospheric pressure.* Both Evans[874] and Sundström and Michaels[2197] were able to show that at very reduced O_2 partial pressures (atm. pressures below 350 mm Hg) hypertrophy of the adrenal cortex originates.

In view of the many physiological processes affected by the adrenal gland and considering the great sensitivity of the adrenal gland to meteorological changes in the environment, it is clear that weather might act as a trigger for many physiological and pathological phenomena, provided these processes have reached a stage close to the morbidity limit of the particular organs.

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* As a criterion for the capillary resistance Regli took the suction pressure required to cause 1–4 petechiae, during a suction period of 1 minute, at the regio supraclavicularis (bone in front of the upper thorax).

5. *The Pancreas*

General anatomy, blood and nerve supply

The fifth important ductless glans which will be discussed in relation to meteorotropism in the pancreas. It is a lobulated gland located transversely across the abdominal cavity at the level of the stomach.

Anatomically it consists of three parts: the *head* (broad right-hand portion of the gland situated against the duodenum, the first portion of the small intestine), the *body* (mid-portion of the gland) and *tail* (tapering extremity extending towards the spleen). In adults the whole gland is about 25 cm long and weighs about 50-160 g.

Functionally it is divided into two parts: an *exocrine* portion composed of pyramidal epithelial cells which secretes the pancreatic juice through pancreatic ducts into the duodenum and an *endocrine* portion consisting of cells scattered throughout the gland, the *islands of Langerhans,* responsible for the production of *insulin.* The islands consist of small clumps of ductless epithelial cells scattered among the ordinary alveoli of the pancreas. They are supplied by large capillary vessels and receive their nerve supply from the vagus (parasympathetic nervous system). They are responsible for insulin secretion which facilitates the combustion of glucose (blood sugar lowering action), stimulates formation of glycogen in liver and muscle and inhibits glucose formation in the liver. Pancreatectomy leads to increased size of the liver (see p. 286), marked decrease of glycogen content and excess of glucose and fats.

Two pancreatic ducts are distinguished: the *Wirsung's duct* (main duct), which usually empties into the common bile duct near its entrance into the duodenum, and the *Santorini's duct* (accessory duct), which is connected with the duodenum at a point approximately 1 inch above the orifice of the common bile duct.

Blood supply: The gland receives arterial blood from branches of the hepatic, superior mesenteric and splenic arteries.

Nerve supply: Stimulation of myelinated fibres from the vagi (parasympathetic nervous system) causes increased secretion of pancreatic juice. Also the islands of Langerhans receive a rich innervation from the vagi causing increased insulin production (see p. 257) followed by lowering of the blood sugar level. The latter vagi stimulation is due to changes in the blood sugar level which affects the hypothalamus, pons and medulla, causing a stimulation of the parasympathetic nervous system. Still the main secretory activity of the islands is regulated directly by the blood sugar level. Apart from the vagi, the principal nerve supply of the gland seems to take place by unmyelinated fibres from the celiac plexus (a network of abdominal nerves).

Functioning and physiological effects

On p. 257 it was pointed out that the functioning of the islands (insulin production and amount of islands tissue) is greatly increased by hormones secreted by the anterior lobe of the pituitary, called the *pancreaticotrophic factor*. This may be a compensatory reaction of the pituitary if the blood sugar level rises too much. The increased insulin secretion lowers this level again. On the other hand, if the blood sugar level falls too much, orthosympathetic nerve stimulation with adrenalin secretion and excretion of the diabetogenic hormone (see p. 257) will cause an outpouring of glucose from the liver (see p. 286), both from preformed glycogen in the liver and from non-carbohydrate sources.

Influence of meteorological factors

Recent studies by Brezowsky and Hansen at the Pharmacological Institute of the University of Munich have clearly demonstrated the influence of changing weather conditions (affecting the temperature and humidity of the environment) on the lowering of the blood sugar level of rabbits after insulin injection. It was found that during influx of humid, warm airmasses the blood sugar level of unfed animals was lowered to a greater extent than during cold-humid or cold-dry weather conditions. However, in normally fed animals the opposite effects were observed.

In view of the mechanism affecting the functioning of the pancreatic gland, it is evident that a meteorologically induced dysfunction of the hypothalamic-pituitary system may affect the functioning of the pancreas and the various physiological mechanisms controlled by this gland. The following considerations may explain this point more fully. On p. 257 we described the various processes controlled by the islands of Langerhans. A dysfunction of pancreatic juice secretion as well may, however, cause a number of pathological phenomena.

The *pancreatic juice* is an alkaline viscous fluid (pH 8.4) which consists of proteins (albumin and globulin) and three main enzymes, trypsin, lipase and amylase. It has an alkaline reaction because of the presence of 0.3-0.65% of $NaHCO_3$ which neutralizes the gastric acid. The secretion in 24 hours is estimated to be 500-800 cc containing 8 g of NaCl. *Trypsin* breaks down proteins into polypeptides and may even liberate amino-acids (leucine, tyrosine etc.). *Lipase* splits fats into glycerol and fatty acids; the activity of the enzyme is greatly increased by bile. *Amylase* converts all forms of starch into maltose. Intake of food creates a reflex stimulation of the vagi (from the mouth), leading to increased pancreatic secretion. The introduction of 0.5% HCl, fat or bile into the duodenum produces the same increase in pancreatic juice secretion; alkaline substances have an inhibiting affect. It is very likely that the pancreatic response to acid is due to a hormone *secretin* (a polypeptide), which is liberated from the intestinal mucosa.

Pancreatic juice liberated by the vagus is viscid and rich in enzymes; the secretin juice is more watery, highly alkaline and poor in enzymes. Meat creates a "secretin" type of response in the stomach, milk a "vagus" type, bread a mixed reaction.

This brief picture of the very complex processes in the duodenum with its own glands (Brunner's glands), juices and enzymes, although much simplified for the reader, may help to explain the complex meteorotropic effects of weather and climate on the physiological processes in the stomach and intestines.

Subsect. E. FUNCTIONING OF THE SPLEEN, LIVER AND GALL BLADDER

As a number of meteorotropic phenomena, to be discussed in Chapter 2 of this Part, are related to the functioning of these organs, a very brief review will be given in this section of the principal physiological processes controlled by these organs.

1. *The Spleen*

General anatomy

This important, large, gland-like organ is situated in the upper part of the abdominal cavity on the left side, lateral to the cardiac end of the stomach. Although it is a ductless organ, it is not a typical ductless gland because so far no specific hormones have been demonstrated with certainty. The spleen is covered by a capsule containing fibrous tissue and unstriped muslce. These muscle fibres contract several times per minute, squeezing blood (brought in by the arteries) out of the spleen and driving it towards the liver.

Functions of the spleen

(1) *Reservoir for blood.* Due to the mechanism just described the spleen acts as a reservoir which can be called upon to augment the volume of the blood if the need arises (*e.g.* anoxia, see below).

(2) *Blood formation.* This takes place during the later months, more especially, of foetal life. The formation of red blood corpuscles and lymphocytes may continue in post-natal life particularly during anaemic conditions of the body.

(3) *Blood destruction.* In the intervening tissue between the arteries in the spleen, called the *splenic pulp,* large amoeboid, mononuclear phagocytic cells (*i.e.* cells which are able to destroy micro-organisms or harmful cells) occur. These *macrophage cells* (which are part of the reticulo-endothelial system) are believed to destroy red cells and blood platelets. From the broken-down haemoglobin bilirubin is formed (see p. 200). In the event of over-activity of the spleen *(hypersplenism),* excessive destruction of blood platelets, granulocytes and red-blood cells takes place.

(4) *Defence against infections.* Poisonous substances affect the macrophages. The amount of immune bodies formed by the body decreases. Splenectomized animals, for example, cannot be immunized against tetanus toxin. Bacteria or other parasites are absorbed with great rapidity by the macrophages. It is evident that the spleen plays an important part in various kinds of infectious diseases.

Nerve supply of the spleen

Motor fibres of the orthosympathetic nervous system reach the spleen and cause it to contract and discharge red corpuscles stored in it. In cases of anoxia, stimulation of the central nervous system causes a flow of impulses along the orthosympathetic nerves to the spleen and adrenal medulla, leading to adrenaline secretion followed by contraction of the spleen and emptying of the filled blood sinuses.

Influence of the spleen on meteorologically induced fluctuations in blood cell counts

Various studies (see p. 314) have produced evidence to show that the number of erythrocytes, leucocytes (both total number of granulocytes, eosinophils, lymphocytes and monocytes) and thrombocytes varies from day to day. But changes in the general level of the blood count during longer periods of the same month and at different seasons have also been observed and they seem to be closely related to certain meteorological factors affecting temperature and cooling. *E.g.,* it was found by Tromp[1305] that in the Netherlands the total number of granulocytes, lymphocytes and thrombocytes reaches a maximum around April (in 1958 at least) and a minimum around August; the amplitude of daily fluctuation is greatest in winter and early spring; the number of leucocytes and thrombocytes suddenly increases during periods of active cold-front passages and influx of cold polar air masses, particularly if they are accompanied by great atmospheric turbulence. These short-term changes, above all, are difficult to explain by sudden changes in the production or destruction of various blood cells. It seems more likely that these changes are created by the absorbtion or release of existing blood cells.

We have seen that the spleen plays an important part in the regulation of the blood composition. It acts as a storehouse for reserve red blood corpuscles, and leucocytes. It was pointed out that the muscles of the spleen receive motor fibres from the orthosympathetic nervous system. Stimulation of these orthosympathetic fibres causes the expulsion of blood cells stored in the spleen. The fluctuations in the number of blood cells in the blood stream seem to be due to the storage of these cells in the spleen and in the blood capillaries where the circulation is sluggish. With increased activity of the blood stream they will be released and reach the main blood stream again, which means to say that any environmental factor affecting the circulatory conditions is liable to increase or decrease these tendencies. This might explain why the number of leucocytes increases as a result of *exercise* (if carried to the point of fatigue, it may increase up to 300%), *adrenaline secretion* (by the orthosympathetic nervous system) and *mental stress* (having a similar effect as adrenaline secretion). The number of thrombocytes decreases if the spleen is over-active (hypersplenism). As cold stress leads to increased adrenaline secretion and rise in blood pressure (see p. 192), we might expect to find an increased number of leucoyctes and thrombocytes in the blood stream after cold fronts, polar air influxes and during the cold season. This is exactly what we have found. Rise of temperature in the atmosphere and decreased adrenaline secretion will cause a swelling of the spleen and reduction of the number of leucocytes, etc., released by the spleen.

2. *The Liver*

General anatomy

The liver is the largest organ of the body and is situated in the upper, right-hand, part of the abdomen. Its weight and composition may vary according to the diet ingested. It consists of a number of lobes subdivided into lobules. The latter are composed of ramified columns of hepatic cells. Small ducts between these cells contain the *bile,* secreted by tiny vacuoles in the interior of the hepatic cells and discharged into the ducts. The portal vein and hepatic artery enter the liver and supply the liver cells with blood.

Functions of the liver and influence of meteorological factors

(1) *Storage of various substances.* Glycogen (which can be readily converted into glucose and *vice versa*), formed from the end products of carbohydrate digestion (glucose, etc.), lactic acid (liberated from the muscles), etc., fats, serum proteins (dysfunction of the liver may inhibit the increase of fibrino-

gen in the blood serum in the course of infectious diseases), vitamins (e.g. vitamin A in liver fat), haematinic principle (an unknown substance in liver extract during pernicious anaemia), etc.

(2) *Synthesis of various important substances.* Both plasma proteins* (fibrinogen approx. 0.25 g/100 cc blood, globulin 2.7 g, albumin 4.5 g, prothrombin 40 mg, total plasma proteins about 6.5–8.5 g/100 cc) and heparin (a powerful anticoagulant, secreted by the *mast cells,* which are often found in clumps near the walls of small blood vessels, see Riley[534]) are synthesized in the liver. A decreased total protein content of the blood serum may indicate a dysfunction of the liver; also a lack of prothrombin may arise from dysfunction of the liver, prolonging the bloodclotting time (see also p. 318). Both the heparin and prothrombin controlling action of the liver gives this organ a key position in various *blood-clotting diseases* of which some at least are seriously affected by meteorological factors (see p. 319). The influence of the adrenal gland on albumin production and of the thyroid gland on globulin production was previously discussed on p. 268.

(3) *Production of bile.* The production is affected by the ingestion of food, injection of secretin (see p. 283) and vagus stimulation, all three causing an increase in bile secretion. The production is about 500–1000 cc/24 h.

(4) *Role in red blood cell formation* (particularly in pre-natal life) *and destruction.* The *bilirubin* (see pp. 200 and 284) left after destruction of haemoglobin in the spleen, reaches the bile capillaries, where it is oxidized to *biliverdin.* This reaches the intestines, where it is reduced by putrefactive organisms into *stercobilin,* some of which is excreted in the faeces, while some is re-absorbed and, after passing through the liver, is excreted in the urine as urobilinogen. This is converted to urobilin by exposure to air and light.

(5) *Role in carbohydrate metabolism.* The liver can form glucose from carbohydrates but also from non-nitrogenous residues of many amino acids and perhaps also from fats. Hence, the liver holds the key to the *regulation of the blood sugar level.* If the blood sugar rises, glycogen is stored (see above) and *vice versa.* The brain, more than any organ, depends on the blood-sugar level for its energy. Hypoglycaemia therefore affects the brain, creating a feeling of extreme hunger, fatigue, anxiety, excitability, vasomotor disturbances (*e.g.* profuse perspiration), etc. In chronic diabetics, with high blood sugar level due to shortage of insulin, a sudden reduction in blood-sugar level may create similar phenomena. A decrease in the blood-sugar level of the brain leads to increased orthosympathetic discharge of the liver and adrenal

* In healthy adult males in the Netherlands the average percentage distribution is as follows: albumin 69-70%, globulin-α_1 4.5–5.0%, globulin-α_2 5.0–5.5%, globulin-β 8.0–8.5%, globulin-γ 11.0–11.9%. The albumin percentage is highest in winter, lowest in summer.

medulla. These impulses and adrenaline secretion increase the glycogen breakdown into glucose. As the blood-sugar level affects the secretory activity of the islands of Langerhans and of the anterior lobe of the pituitary (*i.e.* the discharge of insulin and diabetogenic hormone) both organs are affected by the liver function. On the other hand, the conversion of liver glycogen is affected by a number of factors: muscular exercise and exposure to cold increases the formation of glucose; stimulation of the orthosympathetic nerves, injection of adrenaline, thyroxine and extracts of the anterior lobe of the pituitary lower the liver glycogen and increase the blood sugar level. In other words, there can *hardly be any appreciable change in the meteorological environment,* affecting the hypothalamic-pituitary system, *which will not have its impact upon the liver and the physiological processes it controls.* This statement is supported by recent investigations of Cook[602]. He studied the effect of reduction in body temperature on cellular function in a group of mice, placed to the neck in an ice bath of 2–5° C for about 30 minutes, lowering the body temperature 15° C. It was observed that the respiratory rate of the liver is significantly elevated by reduced body temperature, the metabolic rate of the kidney cortex was reduced. The change in liver function could still be observed 7 days after the immersion. The process may be due to increased enzyme activity, increased permeability to exogenous glucose, etc. Also the quantity of ether-extractable lipids of the liver seems to increase after hypothermia.

(6) *Role in fat metabolism.* The fat content of the liver increases as the result of a fatty diet and anterior pituitary extracts; it decreases with choline and food rich in protein. After the digestion of fats, the saturated fatty acid constituents are often converted in the liver into unsaturated ones. The fats are broken down into the *ketone bodies,* aceto-acetic acid, β-hydroxybutyric acid and acetone. Cohen[177a] reported recently on the *effect of cold exposure on hepatic acetate metabolism.* In this experiment a study was made of the intermediary metabolic responses on the molecular level of surviving liver slices of adult male rats ($3^1/_2$–6 months of age) exposed to cold stress near freezing temperatures during periods of 1–10 days only. For this purpose the changes in pattern of $^{14}CO_2$ production and fatty acid synthesis from labeled acetate were studied. The following results were obtained: (*i*) After 1 day cold exposure, the ability of liver slices to oxidize acetate to $^{14}CO_2$ or to utilize acetate for the synthesis of cholesterol was not changed significantly, but there was a marked depression in fatty acid synthesis (lipogenesis) and a marked lowering of the livercarbohydrate content, the values being about 1/3 of the control animals. (*ii*) After 5 and 10 days' cold exposure the ability of liver slices to oxidize ^{14}C acetate to

$^{14}CO_2$ was significantly increased due to cold adaptation; (*iii*) After 5 days rats had a tendency for increased cholesterogenesis; they showed a greatly improved lipogenesis in comparison with 1- and 2-day "cold" rats; the liver carbohydrate content rose, being about 60% of the "control" rats. These results suggest an adaptational process at the molecular level. (*iv*) There seems to be a correlation between lipogenesis and hepatic carbohydrate content. When the latter falls below 3%, fatty acid synthesis is negligible; above this level there is a linear function.

(7) *Role in protein metabolism.* The digested proteins in our body break down into amino acids. Via the intestines they reach the liver, probably by diffusion, and from there some of them reach the tissues (the average amino acid-level of the blood is 3–5 mg/100 cc, rising to 10 mg/100 cc after a meal). A portion of the amino acids undergoes deamination, *i.e.* NH_3 is liberated and a non-nitrogenous residue is left, which can be converted into glucose (see above); NH_3 is converted into urea.

(8) *Protective and detoxicating function* (*e.g.* in the taking of drugs or certain alkaloids, or anaesthetics). Thus the degree of toxicity of drugs depends largely on the liver (see p. 585). In many instances, when the liver contains sulphuric acids (produced by oxidation of sulphur-containing amino acids in meat, such as cystine, methionine), the toxins are changed into less harmful sulphates. High protein and carbohydrate but low fat content of the liver (or, diet) therefore *increases this detoxicating function of the liver.*

Higher control centres of the liver

In the previous section various control mechanisms have been discussed: *nerve* control by the orthosympathetic nervous system (see above); *neurohumoral* control by the pituitary (see p. 257), thyroid (see p. 266), adrenal gland (see p. 277) and pancreas (see p. 281) and indirectly by the hypothalamus; *meteorological* control, in particular the abrupt changes in temperature and cooling of the environment.

This brief summary of the function and control of the liver may indicate sufficiently the great importance of this organ in a large number of *physiological* processes which are seriously affected by the changing meteorological conditions of our environment.

3. The Gall Bladder

General anatomy

This pear-shaped body below the liver is a reservoir for bile with a maximum capacity of about 50/cc, the bile being 6–10 times as concentrated as in the hepatic ducts (see p. 285). The common bile duct joins the pancreatic duct near the duodenum. It is closed by Oddi's sphincter.

Composition of bile

Bile is an alkaline fluid containing inorganic salts (*e.g.* $NaHCO_3$) and four principal organic substances: the bile pigments, the bile salts, cholesterol and lecithin, and mucin.

(1) The *bile pigments* are bilirubin (see pp. 200, 284 and 286) and biliverdin which reach the bile channels from the spleen and liver.

(2) The *bile salts* are probably formed in the liver. They consist of equal amounts of sodium glycocholate (a compound of cholic acid, a sterol) and sodium taurocholate (a compound of taurocholic acid $CH_2{\cdot}NH_2{\cdot}CH_2SO_2OH$), which keep the cholesterol of the bile in solution. The excretion of bile salts decreases with fasting and a carbohydrate-rich diet. It is raised by diets rich in proteins. The bile salts facilitate the digestive action of all pancreatic enzymes (see p. 282) and promote absorption of vitamin D and vitamin K (important for maintaining a normal plasma prothrombinlevel and therefore normal coagulability of the blood, see p. 318). The bile salts secreted in the small intestines are reabsorbed and carried back to the liver, where they stimulate the liver to secrete more bile.

(3) *Cholesterol* is a sterol, its main source being yolk of eggs, liver, kidney, butter, etc. It is found in most cells of the body, usually together with *lecithin.* The normal blood level is 0.15-0.2%; it decreases during acute infectious diseases and is raised during thyroid deficiency.

Control of bile secretion

(1) As indicated on p. 286, bile secretion in the liver is increased about 3 hours after the ingestion of food, by the injection of secretin, by reabsorbed bile salts and after vagus stimulation. It slightly decreases at night.

(2) The gall-bladder contracts after adrenaline or orthosympathetic stimulation, but neither vagus stimulation nor secretin or HCl has any effect. The strongest contraction occurs in the presence of large amounts of fat in the intestine (particularly egg yolk), causing complete emptying of the bladder. Extracts of the mucosa of the small intestine (*cholecystokinin*) do the same. Magnesium salts seem to cause a tonic contraction of the gall-bladder and relaxation of the sphincter.

Dysfunction of gall bladder and influence of meteorological factors

(1) Disorder of metabolism may cause high choletserol excretion in the bile (*e.g.* during thyroid deficiency) together with diminishing bile salt

secretion, causing precipitation of cholesterol and leading to cholesterol gall-stones. Calcium precipitation also occurs after secondary infections. Stones of bilirubin and calcium are likewise known. The stones obstruct the bile duct. Sudden strong stimulation of the orthosympathetic nervous system by psychological or meteorological stress will sometimes bring on gall-stone attacks.

(2) The close interrelationship between the gall-bladder and function of the liver accounts for the reflection of most meteorotropic effects of the liver upon the gall bladder, affecting the metabolic processes in the intestines, blood coagulability, and so forth.

Subsect. F. BREATHING MECHANISM

1. *Respiratory Centre and Mechanism of Breathing*

The gray matter controlling respiratory activity is called the *respiratory centre*. It is located in the pons Varoli and in the upper part of the medulla oblongata (see p. 188). The nerve cells comprising the centre are not localized in one compact mass, but are scattered throughout the gray matter of the upper medulla and lower pons. Only complete integrity and coordinated activity of this region of the brain-stem makes normal breathing possible.

Causes of stimulation of the respiratory centre

(1) Small increases in the carbon dioxide-tension of the blood augment the activity of the respiratory centre. Changes in oxygen tension and hydrogen ion concentration are less effective.

(2) Owing to alternate inflation and deflation of the lungs, afferent impulses are created which reach the respiratory centre by way of the vagus (parasympathetic nervous system), the receptors of which are located in the most distensible part of the lungs, probably the alveolar ducts.

(3) Under normal conditions the impulses which reach the respiratory centre by way of nerves pertaining to the tongue and pharynx (from the *carotid plexus* arising in the superior cervical ganglion) have little effect. The same applies to impulses of the vagus from the aortic arch. However, under deep anaesthesia or anoxia chemo-receptors of the carotid and aortic bodies are stimulated by the decrease in oxygen and the increase in carbon dioxide and hydrogen ion concentration in the blood and create greater activity of the respiratory centre. Other impulses reaching this centre may affect the rhythm but are not essential in normal breathing.

Effect of stimulation of the respiratory centre

Nerve fibres from the centre pass in the cervical and thoracic segments of the spinal cord supplying the muscles of respiration which create the changes in size of the thoracic cavity.

2. *Regulation of Breathing*

The regulation of respiration serves several important physiological processes:

Supply of oxygen to the blood and discharge of carbon dioxide

Under normal conditions this pulmonary ventilation is directly proportional to the *metabolic rate.*

(1) *Influence of CO_2 stimulation.* If the partial pressure of CO_2 in the inspired air exceeds that of alveolar CO_2 in the lungs, it becomes increasingly difficult to eliminate the excess of CO_2 in the blood. It was pointed out on p. 87 that the normal atmosphere contains only 0.03% CO_2. According to Campbell, Douglas, Haldane and Hobson, an increase of 0.22 vol.% in CO_2 content of alveolar air (which corresponds to a change of 1.5 mm in tension of CO_2 in the alveolar air), may be enough to double the alveolar ventilation. Both air respiration is stimulated and the volume of air breathed per minute is increased. According to Haldane (1919), even 1/20th of 0.3% may produce distinct breathing effects. As the tension of CO_2 in the arterial blood, to which the respiration centre is exposed, is equal to that in the alveolar air, further increase of CO_2 in the inspired air (up to 9%) increases the pulmonary ventilation proportionally. After 9% CO_2 a decrease in ventilation will take place.

(2) *Influence of oxygen stimulation.* According to Haldane and Priestley, oxygen reduction has a stimulating effect only when it has fallen to about 13%. According to Ellis this threshold value is 18%. As pointed out on p. 293, the actual change in oxygen content of the air at higher altitudes (*e.g.* on mountains) is negligible.

(3) *The ratio between CO_2 output and oxygen consumption.* This ratio for a given time, known as *respiratory quotient,* depends on a number of factors *e.g.* the diet. With pure carbohydrates the ratio is 1; with pure fat it is approximately 0.7; with pure protein 0.8.

Regulation of H-ion concentration of the blood

The slightest changes in pH affect the breathing mechanism and therefore all related processes (see below). Pulmonary ventilation depends therefore on the acidity of the blood.

Regulation of oxygen tension under conditions of anoxia

Regulation of body temperature through metabolic processes

3. *Influence of Acidity of the Blood*

As stated, breathing is very sensitive to small changes in the H-ion concentration of the blood, which depends mainly on the amount of CO_2 present in the blood. The pulmonary reaction always changes in a manner calculated to restore the blood reaction to its normal value; *e.g.*, a rise in acidity (acidaemia) increases the pulmonary ventilation. This increased ventilation results in greater elimination of CO_2, a drop in alveolar CO_2 partial pressure, lowered arterial H_2CO_3 content and therefore lower H-ion concentration.

Acidaemia and the breathing response is brought about by a number of factors: secretion of alkaline digestive juices (pancreatic juice, see p. 282, bile etc.) causing excretion of sodium bicarbonate and excess of H-ions in blood; a meat diet giving H_3PO_4 and H_2SO_4 products causing acidaemia; ingestion of NH_4Cl (the NH_3 splits off and combines with carbonic acid to form urea, the HCl being liberated); excessive breakdown of fats in diabetes mellitus. All these processes cause a rise in respiratory quotient.

Alkalaemia, accompanied by diminished pulmonary ventilation and rise in CO_2 partial pressure of the alveoli, is caused by gastric secretion (HCl being eliminated from the blood), ingestion of $NaHCO_3$, vegetable diets. The same may occur after vomiting or severe intestinal obstruction. The bicarbonate content of the blood increases; the respiratory quotient decreases.

The favourable effect of high acidity of the air on asthmatic patients was mentioned on p. 99 (studies by Tiefensee and others). Part of this effect may be related to the processes just mentioned; and the effect of cold stress on asthmatics (see p. 469) may be, at least partly, associated with these phenomena. We have seen that cold stress is accompanied by increased orthosympathetic stimulation, adrenaline secretion, increased glycogen breakdown into glucose in the liver, followed by a rise in the bloodsugar level. All these processes affect the H-ion concentration of the blood and the pulmonary ventilation (see also pp. 193 and 201; studies of Hoff).

4. *Effect of Oxygen Stress (Low Atmospheric Pressure)*

Oxygen and carbon dioxide content of blood at different altitudes

Under normal conditions, the person being completely at rest, the oxygen requirement is approximately 240 cc O_2/min. The pulmonary ventilation is about 6 l/min. in males, 4.5 l/min. in females. Roughly 4 cc of oxygen out of every 100 cc of inspired air, are absorbed in the blood.

The carbon dioxide content of normal arterial blood varies between 45 and 56 cc; in mixed venous blood, with the subject at rest, it is a few cc higher, rising to 65 cc after strenuous exercise. The CO_2 is a present in the blood in simple solution (as H_2CO_3), as bicarbonate ($NaHCO_3$ in plasma and $KHCO_3$ in the corpuscles) or combined with haemoglobin as carbamino-haemoglobin. Whereas in normal water the solution of CO_2 to H_2CO_3 is a slow process, due to the enzyme *carbonic anhydrase* present in the red blood corpuscles, this reaction is enormously accelerated.

One is often inclined to think that the oxygen content of the air decreases with altitude. As mentioned on p. 291, it is not correct to speak of oxygen lack, but the partial oxygen pressure in the inspired air is reduced at greater altitude. The oxygen concentration hardly changes with altitude. At sea level, with an atmospheric pressure of 760 mm Hg, the percentage of oxygen in the alveolar air is roughly 14% with a tension of 100 mm Hg. This is 7% less than the O_2 content of the atmosphere (21%), the partial pressure of O_2 of the air being 150 mm Hg. With an atmospheric pressure of 646 mm, the O_2 content is 13.19%, *i.e.* only slightly changed. But the partial pressure is only 78.6 mm Hg. In air compressed to 1261 mm Hg the O_2 concentration rises to 16.79% but the O_2 partial pressure increases to 203 mm Hg.

Carbon dioxide produces a different picture. At sea level the alveolar CO_2 content of a subject under normal conditions may be 5.3% (equal to a partial CO_2 pressure of 37.8 mm Hg). If the subject is compressed in an air chamber to 4,640 mm Hg, the alveolar CO_2 content is reduced to 0.9%, the partial CO_2 pressure increasing only to 41.3 mm. In other words, the *respiratory centre is able to control the alveolar CO_2 partial pressure* under widely varying limits of atmospheric pressure.

Direct biological effects of moderate O_2 stress (max. 4000 m altitude)

Studies on the *effects of altitude* on healthy man have revealed a number of interesting physiological changes[1592-1679]: the pulmonary ventilation, the vital capacity of the lungs (*i.e.* the volume of air which can be forcibly exhaled after a full inspiration) and CO_2 elimination increase (the alveolar CO_2 tension falls); the basal metabolic rate is often increased in the initial stages, but soon it is becoming normal and even decreases; the carbohydrate metabolism is usually not affected, only the protein metabolism, leading to increase in body weight, particularly of the muscles; these various processes are different for people with readily over-stimulated nervous system (see

p. 269); the orthosympathetic nervous system and adrenal gland are stimulated, causing increased adrenaline secretion; the thyroid activity decreases (despite the stimulating effect of increased adrenal function, see p. 273), the effect of the thyrotropic hormone thyrotrophin on thyroxine production by the thyroid (see p. 267) is about 10 times more potent at an altitude of 3450 m than at low altitudes; the heart and pulse rate and blood pressure increase; blood circulation in lung capillaries increases and dilatation of peripheral arteries takes place; from 1500 m upward (according to Gartmann) an increase in blood volume and in blood cell count takes place partly due to release of blood cells by the blood reservoirs, partly due to increased erythropoiesis (see p. 314): first an increase in haemoglobin and reticulocytosis (formation of new young red cells) is observed, followed by an increase in leucocytes and thrombocytes, but a decrease of eosinophils; prothrombin content of the blood is decreased, fibrinogen content increased; the 17-ketosteroid secretion increases; peripheral capillary resistance increases (decreased permeability); dilatation of the smooth muscle fibres of the bronchi takes place, causing a relaxation of the muscle wall; more alkaline urine and less NH_3 is secreted by the kidneys; vitamin D increases (probably entirely a radiation effect); the intra-ocular pressure decreases; the general sensibility of the nervous system increases (at least at medium altitudes with barometric pressure of 550–450 mm Hg; above 3500 m the threshold increases rapidly, in other words a sharp decrease in excitability which may lead to unconsciousness): the rheobase for taste, tactile and eye stimulation is lowered*; the adaptational capacity of the eye to darkness is increased; the patellar reflex limit is lowered; the increased stimulation of the autonomic nervous system shows up particularly in the orthosympathetic nervous system. On p. 298 the influence of high altitude on pathological processes in the body will be reviewed.

After a subject has stayed for some time at high altitudes (or in a com-

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* (1) According to Fleisch and Von Muralt (in 1948) the average diameter of the pupil decreases at high altitude although an increase would be expected due to the increase of orthosympathetic stimulation. However, the increase in sensitivity to the light stimulus in the retina is so strong, that a resultant constriction of the pupil is observed.

(2) According to Fleisch and Grandjean (in 1948) the thresholds for bitter, sour, salty and sweet taste are lowered to about 60% at 4000 m altitude. A tasteless quinine solution at sealevel tastes bitter at Jungfraujoch (Switzerland). This change in taste threshold may be related to a change in thyroid function. Fawcett and Kirkwood presented evidence that taste sensitivity to phenylthiourea and related compounds is due to a soluble enzyme system, *tyrosine iodinase*, in the parotid and submaxillar glands. Recent studies by Fischer and Griffin support this observation. Taste thresholds for 6-*n*-propylthiouracil are limited to salivary thyroid activity. Subjects with low thresholds, *i.e.* "sensitive tasters", dislike more foods as a group than subjects with high taste thresholds.

(3) The mean threshold of the patellar reflex is reduced to 75% of normal at high altitude.

pression chamber with reduced atmospheric pressure), it is usually found that breathing is maintained at a much higher level than normal in spite of lowered CO_2 partial pressure. Experiments at Pike's Peak in Colorado have shown that, after acclimatisation, pulmonary ventilation increased from 10.4 to 14.9 l/min, the CO_2 partial pressure decreasing from 40 mm to 27 mm Hg. This decrease in CO_2 tension creates considerable alkalaemia, for which the kidney compensates by excreting less acid urine and fewer NH_3-salts.

Studies with rats by P. S. Timiras *et al.* [1660a] (recently reviewed by Timiras during the 5th Gerontological Congress in San Francisco, 7–12 Aug. 1960) in the White Mountain Research Station Big Pine, Calif., U.S.A., at an elevation of about 12,500 ft., have revealed a number of interesting permanent and semipermanent physiological changes:

(1) The *body weight* of rats, although normal at birth, was significantly lower from the fifth day of age in the rats of the second filial generation born at 12,500 ft. and who stayed there from birth to 13 months, as compared with controls at sealevel or rats born at sealevel and transferred to 12,500 ft. after 6 weeks. This growth retardation persisted even after descent to sealevel.

(2) The same rats (born at 12,500 ft.) showed a marked *cardiac hypertrophy**, which persisted even after 3 months at sealevel. In the rats born at sealevel, but transferred to 12,500 ft. after 6 weeks, a moderate hypertrophy occurred only after 10 months, which was reversible if the rats were brought to sealevel again.

(3) The *liver and muscle glycogen* decreased at high altitude in both groups of rats. This effect disappeared within 48 hrs if the rats were brought to sealevel. *Heart glycogen* increased at high altitude but remained high if the animals were returned to sealevel.

(4) *Adrenocortical activity* is temporarily stimulated on arrival at high altitude or on descent to sealevel. Thirty-five days old male rats brought from sealevel to 12,500 ft., which were killed 24 and 72 hrs after arrival, showed an increase in weight of the adrenals and a weight loss of the *thymus***, both phenomena being classical signs of stress according to Selye. This increase and decrease respectively could still be observed if the rats were killed after 3 months.

(5) Only 31 % of the rats born at great altitude reach the *age* of normal rats at sealevel.

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* Recent studies by D. Pennazola *et al.* [1629a] at the Institute of Andean Biology in Lima, Peru showed differences in the electrocardiogram of two groups of small children, 350 children born and living at sealevel and 190 at Morococha, about 14,900 ft., (4540 m) above sealevel (mean barometric pressure 444 mm Hg). The children comprised 5 groups: newborn, 1 week to 3 months and 4 to 11 months old babies, children of 1–5 and 6–14 years.

The following observations were made: (*i*) In the newborn (both at sealevel and at high altitudes) the electric activity of the heart showed similar characteristics, *e.g.* an accentuated PQRS deviation to the right in the ECG. Some weeks after birth they developed a definite difference. (*ii*) With age, PQRS shifts developed rapidly to the left at sealevel, while in the high altitude group a marked right PQRS deviation persisted throughout infancy and childhood. (*iii*) In the high altitude group, during the first weeks or months of life, the T loop shifts to a forward position, a characteristic remaining troughout infancy and childhood. (*iv*) In the high altitude group there exists a moderate degree of right ventricular hypertrophy, probably related to the anatomic and functional changes in pulmonary circulation as a result of acclimatization. At high altitudes the chronic anoxia causes a persistent pulmonary hypertension and this seems to facilitate the maintenance of the foetal structure of the small pulmonary arteries and arterioles.

** The thymus is a two-lobed ductless gland in the cavity of the chest, just above the heart, the exact function being unknown. At birth it weighs only 15 g, at puberty about 35 g, decreasing at old age to 15 g or less. Some workers believe that it affects growth and gonadal development. Infections and intoxications seem to cause the thymus to involute more rapidly at older age.

Effect of extreme oxygen stress

Under *extreme conditions of oxygen starvation* inadequate oxygen supply to the heart muscles may cause heart failure; the brain may fail in judgement; there may be inability to carry out coordinated muscular movements, etc. Degenhardt could demonstrate the development of malformations of the vertebral column in newborn rabbits as a result of a few hours of artificially created oxygen deficiency of the pregnant female rabbit. It was found that the degree of malformation depends on the rate of oxygen deficiency and on the day of the experiment. In rabbits the 9th day of pregnancy was most effective, the malformations being due to abnormal cell metabolism of the notochord which induces the pathological development of the vertebrae. Also the localization of malformations, induced by oxygen deficiency, was closely related to the day of pregnancy during which the oxygen deficiency occurred. It was found that vit. E, which is essential for the normal functioning of the reproductive apparatus (*e.g.* the seminiferous tubules), reduces considerably the rate of malformations despite serious O_2 deficiency.

Recent studies by Velasquez at the Institute of Andean Biology in Peru suggest that natives of mountainous regions are better able to tolerate very low pressures than people who live at sea level. These mountain folk were still conscious 15–20 minutes after having been exposed to the pressures prevailing at 30,000 feet.

Effect of oxygen excess (at normal atmospheric pressure)

Oxygen excess at atmospheric pressure, on the other hand, does not change the pulmonary ventilation, metabolic rate or blood pressure; mental activity is not stimulated. However, the same experiment at 4 atm. of pressure creates within an hour faintness, drop in blood pressure, convulsions (*i.e.* involuntary contraction of groups of muscles), decreased cardiac output, cerebral vaso-constriction and the like.

Influence of ozone

The influence of *ozone* has already been discussed at length on p. 90. It seems that oxygen uptake, CO_2 output and general metabolism are diminished in the presence of ozone. It stimulates the olfactory nerves, perhaps due to the formation of nitrogen oxides. It may create acute inflammation of the respiratory tract, the lungs becoming congested and oedematous. According to Hermann, the potassium level of the blood increases, the calcium level decreases.

Carriage of oxygen in the blood

The oxygen-carrying pigment of human blood is *haemoglobin,* the average content at sea level being about 15g/100 cc blood in man. One gram of haemoglobin, when fully saturated, combines with 1.34 cc O_2, the full combining power of blood being approx. 20 cc O_2/100 cc blood, of which only 0.3% is carried in direct solution in the blood. Only 95% of arterial blood is saturated with O_2, the oxygen content being 19 cc. In mixed venous blood it is roughly 14 cc, which may decrease to 3–4 cc during strenuous exercise. The partial pressure of oxygen in venous blood is circa 40 mm Hg, in arteries about 90 mm (alveolar air 100 mm). In resting tissue the partial oxygen pressure is less, around 35 mm. Owing to this difference, oxygen rapidly passes out of the plasma through the capillary wall and tissue fluid to reach the tissue cells. With increased capillary resistance and decreased permeability (during cold stress), this rate of penetration is reduced. The greater the pressure difference (*e.g.* in lungs with 100 mm O_2 tension against 40 mm in venous blood) the more rapidly does the oxygen diffusion take place.

For acclimatization to high altitudes the body needs more haemoglobin. Hypoxia stimulates the red bone marrow and large numbers of reticulocytes are formed. The deeper physiological mechanisms involved are still unknown (further discussed on p. 314). During periods of hypoxia, the Hb content may rise to over 120%, which increases the O_2-carrying capacity of the blood considerably.

5. *The Influence of Temperature on Breathing*

In very warm and moist surroundings, when loss of heat by evaporation and radiation is greatly interfered with, pulmonary ventilation increases to eliminate water vapour which assists in the loss of heat. Alveolar partial CO_2 pressure falls, resulting in alkalaemia which is compensated for by the excretion of alkaline urine. Lavoisier found that a resting man in a cold environment uses more O_2. This was confirmed by Lusk. At 26° C a person was absorbing 24 l O_2/h against 27 l at 12° C, causing a 12% increase in heat production. At very low temperatures this increase is partly due to shivering.

6. *Low Atmospheric Pressure and Water Retention*

Various studies suggest a pronounced influence of low atmospheric pressures on water retention. As far back as 1898 Bouchard[1592a] published an article on this subject. He noticed that a fasting man on a self-registering balance would not decline in weight continuously, but the weight may rise from time to time. Experiments on dogs showed the same. He accounted for this by incomplete oxidation of fat to glycogen:

$$\underset{\text{fat}}{2\,C_{57}H_{110}O_6} + 67\,O_2 \rightarrow \underset{\text{glycogen}}{16C_6H_{10}O_5} + 18\,CO_2 + 30\,H_2O$$

Polimanti[1630a] observed occasional gains in weight in hibernating guinea-pigs followed by abrupt losses. It was shown that this is not due to differences in humidity of the air and hygroscopic properties of the fur. The abrupt loss of weight, after an increase, is often said to be the result of a sudden release of accumulated CO_2 and H_2O.

Hasselbach and Lindhard[1605a] found decreased urine secretion at high altitudes. These observations were repeated by Smith in 1928. Experiments were carried out on small bitches in pressure tanks. The bitches received a fixed amount of water, and were catheterized before and after the experiment to measure the exact 24-hour secretion. The diet was uniform and started several days before the experiment. Similar experiments were carried out on 40 rats. These experiments showed the following results: (*i*) There is a water retention in the bodies of dogs and rats when the atmospheric pressure is lowered 2.6 to 9.8 cm during 12–48 hours; (*ii*) The disturbed water balance is accompanied by restlessness.

This result is important from a bioclimatological point of view because, as pointed out on p. 50, in W. Europe a barometric fall of 3 cm in 24 hours is not uncommon in winter. In the Caribbean Area even larger differences are observed within 24 hours. The effect of water retention on restlessness (if applicable to man) should not be neglected in the study of the influence of weather and climate on the restlessness of mental patients, especially schizophrenics (see p. 537).

7. *Low Atmospheric Pressure and Geographical Pathology*

Studies by Hurtado, Monge and others suggest that the incidence and characteristic phenomena of various low-altitude diseases change in areas high above sea level. The acclimatisation to high altitudes may affect the pathology of the native resident in different ways: (*i*) The hypoxia may be directly responsible for a pathological condition (see phenomena described above); (*ii*) The influence could be indirectly affecting certain physiological processes which play an important part in the general resistance of the body to infectious and other diseases, (*iii*) Hypoxia may affect only the incidence, symptomatology and development of diseases which are also common in low-lying regions.

Hurtado[1614] reported a number of pathological differences between the native Indians of Peru inhabiting the plains and those living at 4540 m (at Morococha): (*i*) At high altitude a certain degree of hypertension in the pulmonary artery is observed in the Indian natives, which affects the right heart*. It appears that hypoxia has a constricting effect on the pulmonary vascular bed (according to V. J. von Euler, and G. Lilijestrand and A. Cournand) and increases the blood volume (according to Hurtado *et al.*). The cardiac output, however, is not increased. This occurs only in newcomers. (*ii*) Chronic mountain sickness or Monge's disease, described by Monge in 1928, will be discussed in more detail by Professor Hurtado on p. 425 (*iii*) Hypertension in general is a rare condition. Of 2206 patients in a well-equipped hospital at 3730 m only 2 suffered from hypertension. (*iv*) The cholesterol level is the same at sea level and at high altitudes. (*v*) Coronary thrombosis and myocardial infarction are very rare in Peru. On the other hand, the incidence in certain places in Switzerland is reported as being very high. This may be due to the greater air turbulence in these places (see later p. 506) (*vi*) High incidence of peptic ulcer although hypochlorhydria and anachlorhydria are common at high altitudes (according to Hurtado). (*vii*) Cholecystitis is common at high altitudes. (*viii*) Leukemia has a very low incidence. Some types of cancer are rather uncommon. This, however, is not statistically certain. (*ix*) High keloid formation (new growth of skin on scars) after superficial interventions is common. (*x*) Sulphadrugs seem to have a reduced safety threshold (see also experiments described on p. 587).

Autopsy studies by Campos Rey de Castro at the Institute of Andean Biology, on 36 natives living at altitudes of 4000 m and who died in accidents revealed that the most constant pathological phenomenon in permanent high altitude acclimatisation is the congestion and dilatation of blood capillaries, particularly in the lungs, adrenal cortex, kidneys and spleen; also a hypertrophy in the muscle of the right ventricle of the heart is common; dilatation of the lung alveoli and their greater volume were observed in all 36 cases; also hyperplasia of the reticular cells in the lungs and spleen are common.

8. *Influence of Body Morphology on Pulmonary Ventilation*

Even amongst healthy men with perfectly normal pulmonary functions, great differences in oxygen consumption can be observed due to differences in personality pattern and body build. The study of the influence of morphological variation on differences in physiological function has been rather neglected in physiology.

* According to recent studies by A. Rotta and A. Lopez in 1959, high altitude increases the diameter of the heart (particularly the right side) causing an increase in pressure of the pulmonary artery. Permanent adaptation of the native population to high altitude, which is accompanied by increased pulmonary ventilation and broadening of the thorax, causes a change in position of the longitudinal axis of the heart which creates a characteristic anomaly in the electrocardiogram.

An interesting study was carried out by Seltzer in 1940. Thirty-four Harvard students were tested and their anthropometric characteristics determined. The subject remained in a recumbent resting position for half an hour before the oxygen intake was determined. The following observations were made: (*i*) With increase in age there is a slight decrease in oxygen consumption. Robinson found the same in 1938. (*ii*) As basal metabolism is highly dependent on size of body mass and surface area, the larger the gross measurements the higher the oxygen consumption. (*iii*) Boys with linear body build and dolichocephalic skull have higher oxygen consumption and higher basal metabolic rates per kg body weight than those with more lateral proportions. The same holds for people with short extremities as compared with people with long ones. The same was observed previously by W. P. Lucas and H. B. Pryor[1621a].

Oxygen consumption is higher if shoulders are narrow with respect to stature or trunk height; if hips are narrow related to stature and trunk height; with small chest circumference in proportion to total body height; with narrow chest breadth as compared to torso height; if thoracic cavity is shorter than length of abdominal cavity. (*iv*) The oxygen intake during excercise indicates the capacity of the individual to supply oxygen to the tissues. In other words, high oxygen intake indicates very efficient respiratory and cardio-vascular mechanisms for supplying oxygen to tissues. On a statistical basis it was found that the greatest capacity for oxygen intake occurs in individuals with linear body, short arms and legs (as compared with total body height), great relative sitting height, narrow shoulders (men) and hips, narrow and flat chests, short thoracic cavity, round heads, short and broad faces, long and narrow noses.

The brief summary given above clearly indicates the many physiological effects of a temporary or permanent sojourn at high altitudes, particularly if we add to the phenomena mentioned above the influence of a different solar radiation spectrum at high altitudes which affects the pituitary, thyroid and adrenal glands (see p. 261) in a manner different from the influence experienced at low altitudes. On p. 419 some of the important acclimatization phenomena at high altitudes will be discussed at greater length by Professor Hurtado.

However, it is not only natural high-altitude effects which are important from a bioclimatological point of view. Experiments in so called *climatic chambers* (also known as compression chambers) have demonstrated the many therapeutic applications of low-pressure therapy. Dr. Nückel and Dr. Lincke will discuss the clinical aspects of this problem more fully on

p. 631 while the technical aspects will be reviewed by Dr. Findlay and Mr. McLean (p. 617).

9. *Mechanism of Dust and Aerosol Penetration in the Lungs*

The physico-chemical properties of aerosols were dealt with on p. 101, followed by a discussion of the pathological effects of air pollution by inorganic particles. Special attention was given to the mechanism of dust penetration into the lungs and to the causes of the pulmonary diseases silicosis, asbestosis, siderosis and anthracosis. Further discussion of these matters in the present section therefore seems superfluous (see p. 113).

On p. 351 we shall discuss the influence of the penetration of air ions into the lungs on certain physiological functions. A few general remarks on the *effect of air ions on mammalian trachea* will nevertheless be appropriate here. In a great number of experiments, since 1957, Krueger and Smith in particular, assisted by Beckett and Hicks, were able to demonstrate a number of physiological phenomena in the trachea of mice, rats, guinea pigs, rabbits and monkeys after treatment with air ions. *Positive ions* slowed down the ciliary rate*, caused contraction of the posterior tracheal wall, exaggerated the response of tracheal mucosa to mild mechanical trauma, induced vasoconstriction in the tracheal wall and increased the respiratory rate. *Negative ions* accelerate ciliary movement, reverse the contraction of the tracheal wall (caused by positive ions), inhibits response of the tracheal mucosa to mild mechanical trauma, produce normal vascularity in the tracheal wall and decrease the respiratory rate. Krueger and Smith found in 1958 that the various biological effects ascribed to negative air ions are actually due to negatively ionized oxygen; the effects of positive air ions appear to be the result of positively ionized carbon dioxide. In 1959 the same authors discovered that negative ions *in vitro* are able to accelerate metabolic reactions catalyzed by the enzyme cytochrome oxidase which may be—partly at least—the deeper cause of the biological effects of negatively ionized oxygen. Very recently Krueger and Smith observed the great similarity between positive ion effects and the physiological effects produced by 5-HT serotonin (5-hydroxy tryptamine). Furthermore 5-HT serotonin causes smooth muscle contraction and vasoconstriction in the tracheal wall and increased respiration. These effects are reversed with

* Cilia are delicate tapering filaments which project from the hyaline border of the epithelial cells of the mucous membrane of the trachea. They assist in pushing dust particles upwards at the rate of 1–2 cm/min. Acids, excess of calcium ions and cold stress slow the movements, alkalies or potassium accelerates the rate of action.

negative air ions. The biological effect of positive ions is explained by Krueger as a release in the tracheal cells of serotonin which is quickly oxidized in the presence of negative ions (see above). For further details see p. 364.

The various mechanisms described in the three separate sections on aerosol penetration, together with the mechanisms reviewed in the previous section on the effects of lack of oxygen, might help to explain a great number of important bioclimatological phenomena to be discussed in the following chapters.

Subsect. G. HIGHEST CONTROL CENTRES OF THE BRAIN

(The structural and functional relations between the rhinencephalon and the hypothalamus, in connection with the integral activity of the brain)

by

J. J. G. PRICK

1. *Introduction*

The close functional connection between the so-called olfactory brain (*rhinencephalon*) and the hypothalamic-hypophysial system, on the one hand, and the integration of the rhinencephalic-hypothalamic-hypophysial system with the most differentiated parts of the telencephalon, *i.e.* the neoencephalon, on the other, necessitate a discussion of a more comprehensive nature, particularly in any bioclimatological analysis which tries to explain the deeper causes of the influence of weather and climate on the physiological and psychological processes of man. The following comments will serve to elucidate this point:

(1) The rhinencephalic-hypothalamic-hypophysial system must be regarded as being the cerebral condition for (*i*) The *autonomic corporal activities, i.e.* the vegetative-somatic, the cardio-vasomotor, the visceral, visceromotor and endocrinal ones; (*ii*) The *unconscious psychic life,* namely of instinctive and unconscious emotional behaviour, including the moods. On these grounds the rhinencephalic-hypothalamic-hypophysial system could be called a visceral or emotional brain, an instinctive brain or the brain of the unconsciousness ("Es" brain); (*iii*) The *consciously experienced feelings and emotions.* Only the highly differentiated parts of the so-called rhinencephalon are concerned functionally with the mediation of these consciously experienced feelings and emotions.

(2) The neo-pallial part of the telencephalon is in the first instance to be considered as the cerebral condition for cognition on a high sensory level and for conscious actional behaviour. This part of the cerebrum is therefore

also termed the *cognitive brain*, the brain serving the relation and communication with the "Umwelt" (relational brain) or brain serving conscious mental life ("Ich" brain). Moreover the activities of the prefrontal part of the neopallium must be considered as the biological condition for the appraisal of experienced feelings and emotions.

(3) Clinical data indicate that, failing proper co-ordination and integration between the cognitive brain and the visceral-emotional brain, the instinctive-emotional life of the subject becomes abnormal and at the same time the autonomic-somatic, cardio-vasomotor, visceral, visceromotor and endocrinal activities deviate from the normal. In these circumstances, moreover, intellectual ability is also liable to be substandard.

It can be inferred from these data that in the optimum of mental and bodily health the autonomic-somatic, cardio-vasomotor, visceral, visceromotor and endocrinal processes, including the unconscious psychic functions (such as instinctive and emotional behaviour)—whose neurophysiological correlate is to be found in the rhinencephalic-hypothalamic-hypophysial system—maintain functional relations with the neocortical projection-fields of the higher senses (including their motor fields) and the connected neocortical association-fields (frontal, parieto-temporo-occipital associative fields). Functionally speaking, integrative activity of the cerebrum implies that on the one hand the highest mental processes, which are mediated on a high cerebral (neocortical) level, permeate and regulate the fundamental psychic activities, while on the other hand the fundamental activities not only support the higher ones but are also in unison with them.

Rhinencephalon (for the anatomy see Fig. 50) means "Nose-brain" *i.e. olfactory brain*. It has become evident that only a small part is actually primarily concerned with the perception of smell. Experimental physiological investigation and clinical observations have shown that only a part of the area formerly known as the olfactory perceptual brain, actually possesses this function (cortex of uncus hippocampi and of the area entorhinalis, amygdaloid nuclear complex). The major part is concerned only functionally with the mediation of those autonomic somatic activities and the unconscious behaviour which are primordially evoked under the influence of chemical information from the milieu extern, without these being gnostically experienced.

Olfactory information, and the same is true of gustatory information —being information of chemical influences from the milieu extern—mediates primarily—*via* rhinencephalic activities—an unconscious, autonomic-omatic, cardio-vasomotor, visceral, visceromotor and endocrinal re-orga-

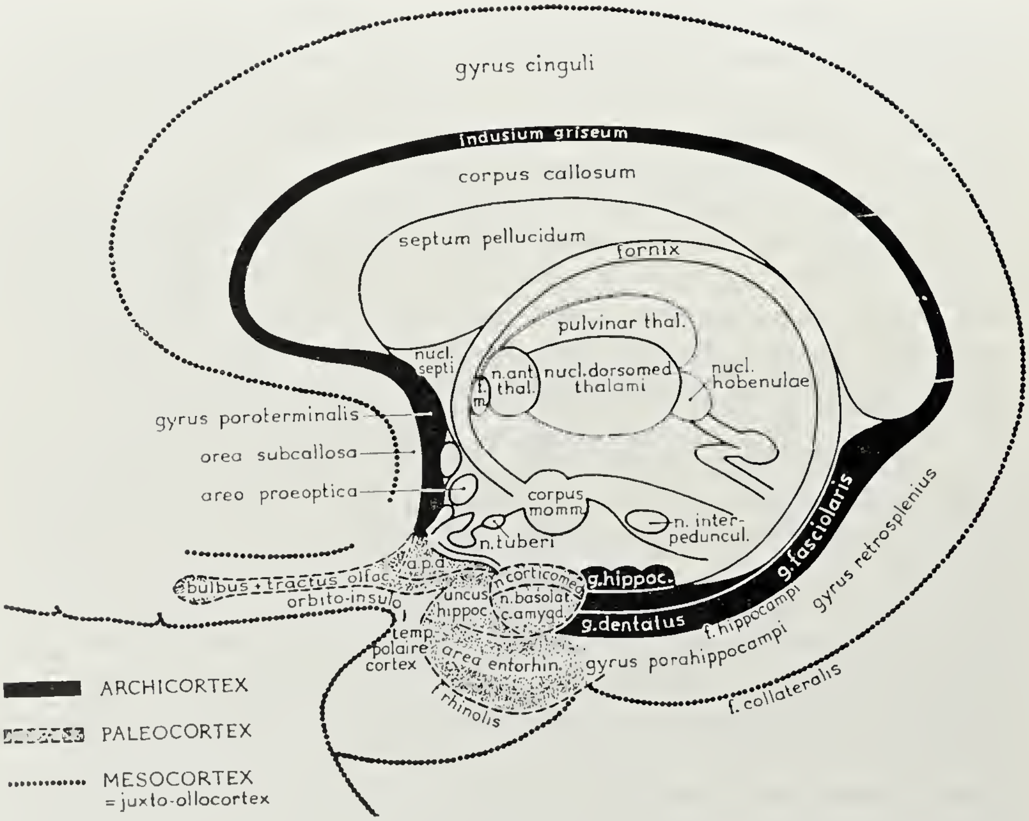


Fig. 50.
The rhinencephalon viewed anatomically.

nisation within the organism, adapted to the operative olfactory and other visceroceptive stimuli.

Man—as a microsomatic being—experiences only a limited number of odoriferous substances on a conscious level as smells. His sensitivity, manifesting itself in the vegatative-somatic sphere, to olfactory and other visceroceptive influences is, however much more extensive than one would suppose when only considering the actual experiencing of smells. Smell, which originally served for the detection of food and the sex partner (and for this purpose is closely linked with sniffing as a particular inhalatory modality), as well as for the appraisal of the milieu extern with regard to its usefulness or danger to the organism, is consequently closely linked with the unconscious urge for self-preservation and preservation of the species. It is therefore by no means surprising that those parts of the so-called olfactory brain, which are not primarily informed of olfactory stimuli, mediate the unconscious instinctive and emotional behaviour, which is necessary for the preservation of the self and the species (hippocampus, septum pellucidum). It should be added in this connection that the amygdaloid nuclear complex and the cortex of the uncus are not only smell-perception areas, but are also concerned with the mediation of instinctive-emotional behaviour.

2. *Divisions of the Rhinencephalon*

The so-called rhinencephalon must be subdivided on functional grounds into:

(1) Smell perception areas (cortex of uncus hippocampi, area entorhinalis and amygdaloid nuclear complex). Further in gustatory perception and other visceroceptive perception areas (fronto-orbito-insular area).

(2) Areas which mediate the unconscious instinctive-emotional life, including the moods. There is no absolute separation of the areas mentioned sub (1) and (2). So we know that the amygdaloid nuclear complex, *interalia,* is, on the one hand, a smell-perception area and, on the other, must be concerned with the mediation of the unconscious instinctive-emotional life. From human pathology we know that the cortex of the uncus hippocampi and the hippocampus in functional relation to the hypothalamic-hypophysial system are also concerned with the (unconscious) instinctive-emotional life and its expressions.

(3) Areas which are concerned with the mediation of certain somatomotor, cardio-vasomotor, visceral, visceromotor and endocrinal activities. In this relation we mention first the gyrus cinguli (pars anterior), the fronto-orbito-insulo-temporo-polar part of the so-called rhinencephalon and a part of the amygdaloid nuclear complex. The orbito-frontal parts of the rhinencephalon (and also the insula) mediate not only some somatomotor, viscero, visceromotor and vasomotor activities, but there exists also in this part a representation of the visceroreceptive nervus vagus, visceroreceptive nervus glossopharyngeus and visceroreceptive nervus trigeminus. We are of opinion, however, that a circumscript topographical representation of the different visceral symptoms and its organs is not realized in the rhinencephalon. Viewed from this standpoint it seems to be justifiable to use the term visceral brain for this part of the so-called rhinencephalon, in which the visceral scheme and the visceral organs are represented.

(4) Areas which mediate the conscious affective experience and its psychomotor expressions (mimicry and pantomimicry). In this connection we mention the gyrus cinguli and area subcallosa. Moreover, the results of

psychosurgery tend to show that the cortex of the orbito-insulo-temporopolar area is also related to emotional behaviour and emotional experiencing.

3. *Normal Physiological Functions of the Rhinencephalon*

After the general remarks above the normal physiological functions of the rhinencephalon should be mentioned.

Perception area for sensory stimuli

The rhinencephalon functions as a perception area for sensory stimuli. In the very first place this is valid for the olfactory stimuli originating from the milieu extern. They are involved in the unconscious reorganisation of our vegetative-somatic, cardiovasomotor, visceral, visceromotor and endocrinal activities. Only a part of this reaches consciousness. Experimental investigation (by J. J. G. Prick) has shown that olfactory information not experienced gnostically, can influence the nature of the secretion of gastric juice and intestinal juice, the gastro-intestinal motor activities and the secretion of saliva. The influence of olfactory information on pancreatic and gall secretion was studied by sounding the small intestine. In addition, these investigations confirmed that, as is well known from everyday experience, olfactory substances, which our consciousness experiences as repugnant (either conditioned or non-conditioned), evoke antiperistalsis of the stomach accompanied by strong secretion of the mucus from the mucus glands of the stomach. The same is true of gustatory impressions and stimuli originating in the viscera, about which the rhinencephalon is also informed (orbital surface of the frontal lobes, insula). Physiological studies have finally shown that somato-sensory stimuli (touch of skin, pain, etc.) and stimuli of other higher senses (visual, auditory stimuli) also converge upon the amygdaloid nuclear complex, which must be considered as a funnelling area, on an unconscious level, for sensory stimuli of the most varied kind.

Somato-motor, autonomic-somatic, cardio-vasomotor, visceral and viscero-motor activities

The rhinencephalon is also concerned with certain somato-motor, autonomic-somatic, cardio-vasomotor, visceral and viscero-motor activities. Both from physiological investigations during brain operations and from pathophysiological data obtained from the clinic, it has been established that stimulation of certain parts of the rhinencephalon is apt to produce respiratory changes. Arrest of respiratory movements has been obtained on stimulating the gyrus cinguli (pars anterior), the posterior orbital surface of the frontal lobes, the insula anterior and the ventro-medial parts of the temporal lobe (particularly the cortex of the uncus hippocampi and of the temporal pole). The arrest of respiration, occasionally interrupted by a deep breath, can be associated, in conscious patients, with a feeling of drowsiness. Inhalations of various vapours may cause the same effect, such as inhibition of respiratory movements.

We know furthermore from clinical experience that dysfunction of these areas often causes the patient to sigh frequently. Tonic contraversive movements of the head and of the eyes are seen during excitation of the rhinencephalic parts of the temporal lobe. Motor-activities, such as sniffing, sucking, licking, smacking, chewing and swallowing, are seen during transient excitation of the nuclear amygdaloid complex and of the septum pellucidum in patients with tumours or traumatic injury of amygdala or septum. Clonic rhythmical movements are induced by stimulation of the amygdaloid nuclear complex during operation, particularly in the facial muscles. Rarely does vocalisation occur. Gastro-intestinal motility can be influenced by stimulation of the amygdala, of the insulo-temporo-polar cortex and of the gyrus cinguli (pars anterior). Such stimulation in animals can induce defaecation and micturation.

Cardiovascular changes can be evoked by excitation of the gyrus cinguli anterior, the posterior part of the orbital surface of the frontal lobe and the temporal pole.

Elevation of the arterial pressure may be induced, but a fall in pressure is also possible.

Post-traumatic cortical damage of these areas often leads to alternation of arterial hypertension and hypotension (poikilopiesis tensiva). Meningeomata of the olfactory area (pars posterior of the orbital surface) are often associated with pronounced arterial hypertension (in our material of cases in 82%).

Pupillary responses, usually pupillary dilatation, are obtained when there is injury to the cortex of the gyrus cinguli anterior, the pars posterior of the orbital surface and, particularly, the cortex of the temporal polar area. This phenomenon is also observed during excitation of the amygdaloid nuclear complex.

Relations to certain endocrinal activities (adenohypophysial gonadotrophic activities and ACTH incretion)

(1) The rhinencephalic influencing of the *adrenohypophysial activities* takes place via the hypothalamus, which is situated between the rhinencephalon and the adenohypophysis. The rhinencephalic influence on the

adenohypophysis is effected by a part of the amygdaloid nuclear complex and the orbital surface of the frontal lobes, as can be deduced from physiological data and particularly from the results of clinical investigation. On anatomical and clinical grounds, it would seem reasonable to assume likewise that the hippocampus influences the adenohypophysial incretions, but experimental physiology has up to now produced few arguments in support of that assumption.

(2) The liberated *ACTH* is known to influence the adrenal-cortex and stimulates the latter to increased secretion of glycocorticoids and of adrenal-androgens (this is also done by LH). The adrenal-glycocorticoids are cortisone and hydrocortisone. These influence the protein-metabolism. Their action on the protein-metabolism is, according to Albright, to be considered as a protein anti-anabolic influence. Cortisone and hydrocortisone inhibit the building up of proteins from amino-acids. Carbohydrates (sugar) and fat can be built up from the desaminated amino-acids. The sugar increase obtained in this way can be described as *gluconeogenesis*. As has been said, ACTH also works to a certain extent as a stimulus to the zona reticularis of the adrenals. As a reaction, an increased liberation of adrenal-androgens takes place, which play a part not only in the contra-regulation of the adenohypophysis but also co-condition the sexual make-up. It is apt to point out here that LH (or ICSH) plays a more important part in the incretion of the androgens than does ACTH. Further it must be remembered that cortisone and hydrocortisone influence the water-salt metabolism, the haematogram, and, finally, the secretion of gastric juice (increased secretion with hyperacidity with a tendency towards the formation of ulcers). It is relevant to this matter that we had on opportunity of examining two cases of traumatic Cushing's disease. In these cases there was no tumour of adeno-hypophysial-basophile cells, but bilateral lesions in the fronto-orbital cortex and in the amygdaloid nuclear complex.

Dysfunction of the rhinencephalon may cause disturbances in the sexual sphere, namely in libido and potency. Of the possible mechanisms involved, two deserve consideration: (*i*) It may be supposed that the hypothalamic nuclear areas which regulate the adenohypophysial-gonadotropic activity (nuclei tuberis laterales) come to dysfunction under the influence of the pathological activity of certain parts of the rhinencephalon (a part of the amygdaloid nuclear complex and the orbital surface of the frontal lobes). (*ii*) From physiological examination we know that lesions of the amygdaloid nuclear complex may cause degenerative changes in the nuclei of the tuber cinereum which regulate sexual maturation (*interalia* the nucleus hypothalamicus ventromedialis).

We had an opportunity of observing several patients who showed hypersexual behaviour after traumatic injury to the orbital surface of the frontal lobes and the amygdaloid nuclear complex. In some other cases with the same localisation of the traumatic lesions there was a complete loss of libido and potency.

Rhinencephalon and stress

The functioning of the rhinencephalon, in so far as it mediates the ACTH incretion, is an important factor in various stress conditions in Selye's sense. Stress is the unconscious answer of the organism to an external or internal (possibly combined) stress-evoking situation, which can be of a biological or an emotional nature, or to situations which are objectively viewed as not normally evoking stress, yet subjectively are evaluated instinctively as such. In these cases, too, the rhinencephalic-hypothalamic-hypophysial system, with its subordinated endocrinal-vegetative system, reacts with a biochemical (endocrinal), vegetative-somatic and biological-psychic stress pattern.

If the stress-causing situation is not held in check by release of the stress, the individual becomes the victim of a so-called adaptation illness. Selye has subdivided and distinguished these as *hyper-adaptation* and *hypo-adaptation diseases*. Examples of the hyper-adaptation diseases are: gastric and duodenal ulcers, as well as essential hypertension. Hypo-adaptation diseases are ulcerative colitis, bronchial asthma, certain psychosomatic skin diseases (some eczemas, etc.), urticaria and Quincke's oedema. Hyperthyroidea, certain forms of prurigo, some rheumatic diseases (*inter alia* primary chronic rheumatoid arthritis), angina pectoris (and subsequent coronary thrombosis) also belong to the adaptation diseases. In the light of the foregoing this means that all these *psychosomatic diseases* (also called *adaptation diseases*) have a neurophysiological correlate on the level of the rhinencephalic-hypophysial-hypothalamic system. This does not, however, by any means imply, that the causal genesis of these diseases is thereby indicated. The adaptation diseases have, in so far as they are psychosomatic aberrants, a multi-conditional genesis. We mean by this, that the causa efficiens is unknown, while several multiconditional factors are found to be involved. One of these factors is the lack of an optimal realisation of the activity of the rhinencephalic-hypophysial-hypothalamic system. This lack can be attributed to a failure in integration of the rhinencephalon with the neoencephalon or to a temporary loss of a previously attained integration of the rhinencephalon with the neoencephalon.

Rhinencephalon and immunity processes

The activity of the rhinencephalon in relation to the ACTH incretion is further involved in the immunity processes. ACTH mediates the liberation of gamma-globulin from the mononuclear leucocytes. Gamma-globulins are either themselves immunity substances or bearers of certain immunity substances. From the fact that the rhinencephalic system influences the ACTH incretion while ACTH is involved in the immunity processes, it follows that links may be assumed *between certain rhinencephalic activities and certain aspects of the immunity processes.*

Mediation of the nature of moods

The rhinencephalon plays a part in the mediation of the nature of moods. The mood, which can be defined as the emotional tonus, is, as far as its nature is concerned, closely correlated with the nature of the vegetative somatic, cardio-vasomotor, visceral and visceromotor activities. As was indicated above, the rhinencephalon is associated with the regulation of the vegetative-somatic, cardio-vasomotor, visceral and visceromotor activities and in this way it is concerned with the mediation of the moods. Moreover the rhinencephalon influences the adenohypophysial ACTH incretion. We know that this hormone must be considered as an euphorising hormone.

Mediation of the instinctive life

The rhinencephalon mediates the instinctive life. This function has been established both by physiological research on animals and from clinical data of human pathology. Firstly we know that animals are largely dependent on olfactory stimuli in their search for food and a mate; hence they serve the preservation of the specimen and of the species. Further, it is a well known fact that ACTH, whose incretion is regulated by the rhinencephalon, is a metabolic hormone and moreover, an immunity-mediating hormone, which is of great importance for the preservation of the individual.

It has been stated that stimulation of the amygdaloid nuclear complex and of the septum pellucidum provokes certain activities such as sniffing, licking, sucking, smacking, chewing and swallowing, whether or not accompanied by secretion of saliva, which activities must be regarded as components of instinctual behavioural patterns which serve both the preservation of the individual and of the species. Preservation of the species is an instinct bound up with the adeno-hypophysial gonadotrophic activity for one thing. We have said already that the rhinencephalon (amygdala, hippocampus, orbital surface of frontal lobes, septum pellucidum) is concerned with the regulation of this activity via the hypothalamus. We know that, in close association with the activity of the hypothalamus, prolactin mediates the behaviour during maternity.

It has been established, both by physiological examination of animals and from clinical data obtained in man, that the rhinencephalon (amygdaloid nuclear complex, cortex of the uncus hippocampi, hippocampus, gyrus cinguli, orbital surface of the frontal lobes) is functionally closely concerned in the conditioning of emotions of fear, anxiety and aggression. These emotions must be qualified as instinctive emotions. The unconscious moods and the unconscious emotional intentionality of man to his world must be considered as the result of his instinctive appraisal of his "Mitwelt". From experiments on animals we know, finally, that certain parts of the rhinencephalon, in close relation with the hypothalamus, mediate instinctive-emotional expressions (*i.e.* septum pellucidum and certain parts of the amygdaloid nuclear complex).

Conscious experiencing of feelings and emotion

The parts of the rhinencephalon with a juxta allocortex (gyrus cinguli, gyrus retrosplenius, gyrus para-hippocampi, orbito-insulo-temporo-polar area, area subcallosa) are concerned with the conscious experiencing of feelings and emotions and their expressions with the aid of the psychomotor activities (mimicry, pantomimic expressive movements and representative expressive movements). It is evident both clinically and from the results of psychosurgical operations, that the juxta-allocortex is concerned with this specific experiencing (on the human level) of the affective and emotional life and its expression.

For the realisation of the emotional expression patterns the parts of the rhinencephalon mentioned, function in integral activity with the hypothalamus. Further one can deduce from the results of clinical examination of patients with disturbances of the juxta-allopallium that this area mediates the integration of the emotional with the cognitive aspects of the psychic life. This implies that the neurophysiological correlates of this integrative activity are primordially tied to the juxta allopallium.

Character and temperament

The rhinencephalic activities, combined with those of the other parts of the ventral telencephalon (including the endocrinal-autonomic system) must be considered as fundamental physiological correlates of the character, including the temperament. Clinical data show that lesions of the orbital surface of the frontal lobe, the temporal pole, gyrus cinguli, uncus hippocampi, amygdala, hippocampus and septum pellucidum, may cause behavioural deviations in man. Although this abnormal behaviour may be transient, it may possibly persist. In such cases the habitual action and reaction patterns are to be regarded as manifestations of a cerebrogenic malformation of character. As is well known, the character can be seen as the complex totality of integrated conative intentionalities of the personality to its world. It follows from what has been stated that the normal structure and functions of the rhinencephalon must be realised to maintain a normal character as an essential factor of the personality structure.

From the neurophysiological point of view it may be said that behavioural disturbances, as manifestations of a malformed character and personality structure, are realised when: (*i*) Under the influence of certain pathogenic factors, the primitive parts of the telencephalon, combined with the hypothalamic-hypophysial system and the other parts of the brain-stem, are structurally and functionally disturbed; (*ii*) The neopallium shows structural and functional disturbances; (*iii*) The functional integration of the rhinencephalon with the neopallium is not realised.

Regulation of the different states of consciousness

The parts of the rhinencephalon which are functionally related to the formatio reticularis—particularly in the mesencephalon and diencephalon—influence the activities of the formatio reticularis as central activating system, and so they are concerned in some way with the regulation of the different states of consciousness. In this connection we mention the amygdaloid nuclear complex, the hippocampus, the septum pellucidum and the orbital surface of the frontal lobes. Both the lucidity and continuity aspects of the consciousness are influenced by the rhinencephalon parts mentioned in relation to the formatio reticularis.

Memory and learning

Clinical data from human pathology suggest that the hippocampus plays a part in the mediation of the memory and via this function is connected with learning processes. Bilateral lesions in the hippocampus with degenerative changes in the fornices correlate with a state of dementia, which is primarily based on a loss of memory. Further, it is well known that the hippocampi maintain a structural and functional relation with the corpora mammillaria via the fornices. Lesions of these corpora mammillaria have as a result amnestic syndromes (Korsakow psychosis). We also know that the corpora mammillaria are closely connected with the mesencephalic part of the formatio reticularis, which mediates the regulation of the conscious processes.

Modulation of functions and behaviour

The fact that stimulation of the same rhinencephalic area can provoke opposite effects suggests that there is no circumscript representation of functions and behaviour in the rhinencephalon. It is reasonable to assume that the rhinencephalon in the first place modulates functions and behaviour, which are integrated in sub-cortical structures (*inter alia,* the hypothalamus).

Manifestations of the unconsciousness

Since the allopallial rhinencephalic areas must be regarded as the cerebral conditions for human consciousness, it seems reasonable to suppose that essential manifestations of the unconsciousness have their neurophysiological correlates in this part of the telencephalon. We are thinking of states like dreams, human telepathic activities, "sentiment du déjà vu", unconscious imagination, ecstasy and so forth. From the standpoint of pathology it is important to know that transient delirious, exitation and twilight states, fugues, exceptional conditions, hypnotic-like situations, unconscious emotional discharge and other primitive automatic states can occur when a dysfunction, caused by lesions in this part of the rhinencephalon, prevails.

Dysfunctions of the rhinencephalon

Finally we are of opinion that certain dysfunctions of the rhinencephalon must be considered as the patho-physiological correlates of many *diseases of clinical psychiatry,* including the *psychosomatic diseases.* In this connection we mention the endogenic depressive psychoses, neuroses, psychopathy, psychomatoses, organic psychopathiform states, schizophrenia, temporal lobe epilepsy (psychomotor epilepsy), symptomatic psychosis, etc. In all these cases the optimal integration of the rhinencephalon with the neoencephalon is not or incompletely realised, conditioned by endogenous or exogenous morbid factors. Consequently the rhinencephalon in a functional unity with the hypothalamic-hypophysial system overrates too autonomically. This means that in all these cases the biological-psychic functions and the autonomic-somatic activities, which are mediated by the rhinencephalic-hypothalamic-hypophysial system, show a lack of the highest regulatory control, and so they are not adapted to the external and internal situation.

Subsect. H. FACTORS AFFECTING THE COMPOSITION AND PHYSICO-CHEMICAL STATE OF THE BLOOD; 17-KETOSTEROID SECRETION; DIURESIS; CAPILLARY RESISTANCE AND PERMEABILITY OF MEMBRANES

1. *Factors Affecting the Composition and Physico-chemical State of the Blood*

During the last 50 years a great variety of experiments has been carried out to study the influence of weather and climate on blood count, haemoglobin content, etc. In order to be able to evaluate these studies, a brief review will be given of the known non-meteorological factors affecting these various biological processes.

Blood cell count

The average *red cell* count in adult males amounts to about 5.5 millions/cc, in females 4.8 millions. Individual variations of 1 million may occur in healthy states and considerable variations during 24 hours are noticed, fluctuations of 10–20% being common. The *white cell* count is on the average 6000–8000/cc (of which 70% granulocytes, 25–30% lymphocytes and 5–10% monocytes), but fluctuations between 5000 and 10,000 are quite common. The average *thrombocyte* count is 250,000–500,000/cc.

On p. 297 (Effect of lack of oxygen on stimulation of bone marrow), p. 283 (Function of the spleen as blood reservoir and its effect on blood formation and destruction) and p. 286 (Function of the liver in blood cell formation and destruction) a number of mechanisms have been discussed affecting the number of erythrocytes, leucocytes and thrombocytes. It was stated on p. 284 that short term variations in the number of blood cells in the blood stream are probably due to differences in release of existing blood cells from the spleen reservoir and from peripheral blood capillaries.

On p. 297 it was pointed out that *erythropoiesis* (formation of red blood cells) is stimulated during hypoxia or anoxia due to stimulation of the bone marrow. At least three more processes are known which seem to have similar effects.

(1) Thyroid deficiency (myxoedema, see p. 268) seems to depress marrow activity and may cause anaemia. Thyroxine does not seem to have a specifically stimulating action on the marrow, but the thyroid acts as a general metabolic stimulant. Considering the various meteorological factors affecting thyroid activity (see pp. 269–274), the logical inference is that these factors may affect general erythropoiesis.

(2) Recent studies by Kennedy and Gilbertsen suggest that androgen hormones (see p. 278) also stimulate erythropoiesis considerably. In anaemic patients the haemoglobin content may increase from 9 to 13 g/100 cc after treatment with testoterone compounds. As androgen production is controlled by the pituitary, environmental factors affecting the pituitary may influence the rate of erythropoiesis.

(3) Recent studies in Israel by Matoth, Biezunski and Szabo likewise suggest the possibility of a humoral stimulation of the bone marrow during

hypoxia by a substance described as *hematopoetin*. Experiments with bone marrow *in vitro* indicated increased erythropoiesis after treatment of the cells with serum of patients suffering from anoxia. However, further experiments are required to confirm these findings.

(4) Some authors believe that vitamin C also has a marrow-stimulating efffect. It was pointed out on p. 264 that vitamin B stimulates thyrothrophin production. Similarly vitamin C seems to have some influence on thyroid activity and therefore on the activity of the bone marrow.

Haemoglobin content

In a later section on seasonal pathology the haemoglobin content of the blood will be shown to undergo long-term (seasonal) changes (high values in winter and low in summer) and short term variations (high Hb values after sudden influx of cold polar air). The latter group of changes can be considerable, the periods of change varying from one to several days.

The haemoglobin percentage of the blood is liable to be increased by any of several known causes:

(1) Increased adrenaline secretion (*e.g.* increased orthosympathetic stimulation due to cold stress) affects the spleen by decreasing its size, causing an expulsion of blood cells in the blood stream, and decreases the blood volume (partly regulated by the spleen), causing a relative increase in haemoglobin. Other factors affecting the blood volume (see p. 323), as well, may cause a temporary change in haemoglobin concentration.

(2) High protein intake. This is important in the formation of the protein globin, which, with the pigment haematin (an iron porphyrin) forms haemoglobin.

(3) Sufficient acid of the gastric juice to liberate food iron in an inorganic form. The gastric juice secretion increases with reflex stimulation of the vagus nerves or after a drop in the blood-sugar level (affected by insulin level and pituitary function, see p. 286), etc.

(4) Sufficient bile secretion to facilitate the absorption of the liberated iron.

(5) Vitamin C has a similar effect as the bile secretion.

(6) Efficient functioning of the thyroid and secretion of thyroxine increases the function of the bone marrow.

(7) Oxygen stress does the same.

(8) Androgen hormones have also a stimulating effect (see above).

Both the actual and relative increase of haemoglobin during cold stress affects the oxygen-carrying power of blood and therefore influences a number of physiological processes in the human body.

Blood sedimentation rate (B.S.R.)

It is generally known that the speed of sedimentation of the red blood corpuscles of the same blood sample (placed in a vertical thin tube), which is kept fluid with an anticoagulant (citrate, oxalate or heparin), may change as the result of a number of technical factors (differences in diameter and length of tubes, composition and pH of anti-coagulant, inclination of tube, temperature, etc.)*. However, even if the influence of these factors is eliminated, differences occur from one day to another which are not only due to pathological causes (*e.g.* infectious diseases, increased cholesterol level of the blood, leucocytosis, etc. increase the B.S.R.).

The mechanism of blood sedimentation is only partly understood. The settling of the corpuscles is resisted by the viscosity of the medium (*i.e.* the lower the viscosity, the greater the rate of sedimentation); the retarding force also varies directly with the surface area of the falling particles.

Cells tend to aggregate and form so-called *rouleaux* (cells piled one on top of the other). As a result, the mass-to-surface-area ratio increases and the particles will sink with greater rapidity. B.S.R. therefore *depends both on viscosity and speed of rouleaux formation,* the latter being partly dependent on the former.

Factors affecting the viscosity of the blood

(1) The composition of the blood serum. Viscosity increases with increased protein concentration. As the major part is composed of albumins, increased albumin will increase the viscosity and reduce the B.S.R.

(2) Salt. An increase in sodium choride usually lowers the viscosity.

(3) The number and size of blood corpuscles. Increased haematocrit values from 25 to 65% increases the viscosity from 1.7 to 3.0 (viscosity of water taken as 1).

(4) The tonus of the sympathetic nervous system. Increased orthosympathetic stimulation increases the viscosity of the blood due to adrenaline secretion, causing a constriction of peripheral arterioles and capillaries and decreased blood volume.

(5) Mental stress. It seriously affects the viscosity of the blood. Levine *et al.*[1281], studying the blood viscosity of both psychotics and non-psychotics under stress, found that both viscosity and coagulation of the blood increase under stress conditions, the rate of increase being roughly proportionate to

* (1) Reduced B.S.R. values are observed if the test is done some time after the blood sample is taken. (2) The test should be carried out at temperatures of about 22° C; increasing temperature raises B.S.R. (3) B.S.R. usually rises with increased length of the tube and increased inclination. (4) Increased dilution of the anti-coagulant accelerates the B.S.R.

the increase in stress. Previously Cannon, Gray and Mendenhall[1292-1295] had discovered that increased adrenaline secretion shortens the blood coagulation time, probably by stimulating the liver to greater activity in discharging some coagulating factor, probably fibrinogen or other related substances. Schneider also found that stress shortens clotting time, the degree of change appearing to be proportional to the extent of elevation of the blood pressure, particularly in patients suffering from hypertension.

Factors affecting the rouleaux formation

(1) According to Fahraeus, plasma proteins, especially those with highly asymmetrical molecules such as globulin and particularly fibrinogen, increase the B.S.R. Cholesterol, polysaccharides composed of large molecules (*e.g.* dextran) and perhaps muco-proteins also usually increase the B.S.R. As pointed out on p. 286, fibrinogen is produced by the liver and the quantities produced are therefore affected by a number of factors like those described on p. 287. It is often stated that fibrinogen is far more conducive to rouleaux formation than globulin, but, as the serum contains approximately eight times more globulin than fibrinogen, the total effect is about the same.

(2) According to Giordano[1283-1286], Parodi and others, rouleaux formation is also affected by the electric charges of the blood particles (both positive and negative). As long as the repellent charges prevail, the particles will remain in suspension but, if they decrease, the force of gravity will have the upperhand and sedimentation take place.

The foregoing summary indicates that decreased B.S.R. may be due to decreased globulin, fibrinogen and rouleaux formation, but the same effect could be obtained by increased viscosity of the blood as a result of increased protein concentration of the serum (particularly of albumin) and of the number and size of blood corpuscles, etc.

The various mechanisms described may help to explain a number of interesting biometeorological observations:

(1) Rodahl[1288, 1289] observed a very high B.S.R. (up to 26 mm during the first hour) in healthy *Eskimos* in polar regions. Their total serum protein level is normal (7.12 g/100 cc), but the mean albumin level is only 49.5% (against 69% in healthy blood donors in W. Europe) and the globulin level 59.5% (against 31% in W. Europe). The serum of Europeans living in these polar regions is also different. The high globulin content may be responsible for the increased rouleaux formation; the low albumin content decreases the viscosity. Both factors favour a high B.S.R. It is interesting to note within this contest that healthy *schizophrenics* often have high blood sedimentation rates and low albumin (or high globulin) values.

(2) Among a group of 5000 healthy blood donors at Leyden (The Netherlands) the following changes in B.S.R. patterns were observed by Tromp[549]: (*i*) The lowest B.S.R. (*i.e.* highest percentage of donors with 1–2 mm B.S.R. during the first hour) occurs in winter, particularly in February. The percentage of donors with 1–2 mm B.S.R. may decrease from 56% in February (1959) to 38% (in June). (*ii*) Short-term fluctuations are also found, *viz.*, low B.S.R. occurs in the healthy population during periods of high haemoglobin values, which are usually characterized by steeply falling environmental temperatures and great atmospheric turbulence (*i.e.* under pronounced cooling conditions).

Blood coagulation and fibrinolysis

Blood coagulation (clotting) is caused by the interaction of the enzyme thrombin with the soluble fibrinogen of the blood plasma (see liver function, p. 286), giving an insoluble protein fibrin*. The coagulation rate decreases with falling temperature. Thrombin is formed from prothrombin (see p. 286) in the presence of calcium ions (see p. 275) and of various substances liberated from disintegrated blood platelets, damaged blood and tissue cells (thromboplastins). The fluidity of normal circulating blood depends to some extent on the presence of heparin, a sulphur-containing polysaccharide (see p. 286). Various other compounds have been discovered which have similar anticoagulant effects, *e.g.* cellulose or glycogen to which SO_4-groupings are attached. For further details we must refer to the many modern studies on blood coagulation, a mechanism much more complicated than the summary given above may suggest.

As mentioned on p. 286, both prothrombin and fibrinogen are formed in the liver. The prothrombin formation is greatly affected by vitamin K intake and absorption. It is present in various diets, *e.g.* spinach, cauliflower, cabbage, etc. Lack of vitamin K lowers the prothrombin level of the blood and greatly prolongs the blood-clotting time. The vitamin K absorption from the small intestine occurs only in the presence of sufficient bile salts (see p. 289). This close interrelationship between liver and gall-bladder function and blood clotting implies that all meteorological phenomena affecting the function of liver and gall-bladder may also affect blood coagulation and the physiological phenomena related to this process.

The opposite to blood clotting is known as fibrinolysis, *i.e.* the spontaneous

* If blood is treated with a 0.1% potassium oxalate solution, the free calcium ions are precipitated as calcium oxalate. The fluid remaining after centrifuging is known as oxalate plasma. By adding an equal volume of saturated NaCl solution, fibrinogen is precipitated. One mg of thrombin can coagulate 100 cc of oxalate plasma at 38° C in 10 seconds.

re-solution of fibrin. The clot softens and, in the absence of bacterial contamination, it goes completely into solution after a period of hours or days. The detailed mechanism is not yet known. According to studies by W. G Tillett and R. L. Garner in 1933 certain streptococci seem to produce a substance called fibrinolysin which causes a rapid destruction of human fibrin clots (not in rabbit blood).

It is compatible with the mechanisms described that blood coagulation and fibrinolysis should be liable to be seriously affected by weather and climate. In point of fact, direct experiments support this assumption:

(1) It has emersed from studies made by Caroli and Pichotka[1296] in 1952 at the Physiological Institute of the University of Freiburg (Germany) that the coagulation time of the blood of rabbits shortens before the passage of warm and cold fronts, though more gradually before the passage of *warm* fronts. After the front has passed the blood-clotting time rises above the normal. A few hours afterwards the values become normal again. *Cold* fronts are also preceded by a fall in clotting time, but it is more pronounced; the lowest value is found shortly before the passage of the front, after it the clotting time rises steeply. These conditions persist for a considerable time, in contrast to those depending on warm fronts. Similar phenomena were observed during thunderstorms.

(2) Studies by Caroli[1242] from May 1948 to October 1949 confirmed the previous observations by Halse and Losznitzer that the fibrinogen content of a group of healthy donors fluctuates with changing weather conditions. It was found that, provided the passages of fronts occurred at intervals of several days, the passage of a cold front is always accompanied by a marked increase in fibrinolysis. The authors were unable to establish significant correlations for warm fronts or occlusions (see p. 19).

(3) Tromp has found that in the Netherlands the highest mortality from arteriosclerotic heart diseases (coronary thrombosis, myocardial infarction, etc.) occurs during the coldest months of the year (January and February), which are also the months with lowest blood sedimentation rates (see above).

It is appropriate to state here that the effect of cold stress may be related to the phenomena described by Cannon and Schneider (see p. 193), *viz.*, that adrenaline secretion as a result of stress shortens the blood coagulation time, probably owing to increased liver stimulation, and that the shortening of the clotting time is more or less proportional to the extent of elevation of the blood pressure as a result of stress.

The meteorotropic relationships found so far require further study, but the few data given sufficiently indicate the great significance of these biometeorological studies in view of the very high mortality from coronary heart diseases in most of the advanced countries.

Acidity, protein spectrum, calcium, phosphate and magnesium level of the blood

The various physiological mechanisms involved in the daily and seasonal changes of these different phenomena have been briefly described in the previous sections, *i.e.*, on pp. 193, 201, 292 (Acidity of the blood), p. 286 (Influence of liver function on plasma proteins), p. 268 (Influence of thyroid and adrenal gland on albumin and globulin production of the liver) and p. 275 (Influence of parathyroid on calcium, phosphate and magnesium level of the blood) The reader is referred to these various sections.

When we come to discuss diuresis (see p. 330), we shall point out that the kidney plays an important part in regulating the hydrogen ion concentration of the blood. With increased acid production in the body, the excess is excreted in the urine. The formation of acid urine is probably affected in the renal distal tubule by the passage of H-ions into the tubule in exchange for Na-ions which leave it. See below.

Sodium and potassium level of the blood

Both elements occur as chlorides, phosphates and carbonates in the body, sodium being the chief cation of the body fluids, while potassium is found chiefly in the intracellular fluids (without chloride). The *influence of adrenal function* on the potassium-sodium ratio is described below and on p. 278.

Sodium

Sodium, chiefly in the form of chloride, plays a leading part in various physiological processes of the body. The amount excreted in 24 hours is roughly 5 g, but it fluctuates largely with the diet.

(1) *Principal functions of sodium.* (*i*) It is required for the maintenance of the proper osmotic pressure of body fluids. For example, the mammalian heart muscle requires a 0.9% salt solution for proper functioning. Sodium chloride acts as a stimulus to contraction of the heart muscles. (*ii*) It is essential in proper concentrations for the normal functioning of the cell.

(2) *Control of sodium chloride level.* (*i*) As explained on p. 232, the principal centre of thermoregulation is located in the *hypothalamus*. As the amount of NaCl secreted by the urine depends to a considerable extent on the thermoregulation processes of the body, it will be evident that the hypothalamus is one of the very important control centres of the sodium chloride level of

the blood. (*ii*) The *endocrine organs* are the chief agents in the regulation of the electrolytic and water balance of the body by affecting the renal functions (see p. 331). The adrenal cortical hormones (aldosterone and progesterone, see p. 278), in particular, increase the absorption of Na and Cl in the proximal renal tubules and aid their retention in the body, the action being opposed by the antidiuretic hormone of the pituitary (see later) which impairs electrolyte retention and augments water reabsorption. Thyroid hormones also support the adrenal function by reducing water reabsorption. As stated on p. 278, adrenal dysfunction decreases NaCl in plasma (probably due to increased excretion in urine) and increases the potassium concentration in the plasma, tissue fluids and tissue cells (probably due to diminished excretion in the urine). As most of the hormonal functions described are largely controlled by the pituitary and hypothalamus, the primary cause of changes in sodium level must be sought in the hypothalamus and parts of the brain affecting this organ.

(3) *Effect of an excessive intake of sodium chloride.* An excellent summary of the effect of excessive salt intake was given by Medway and Kare. Many reports describe death and illness in animals after ingestion of an excess of salt. Also brain lesions have been reported. According to Medway this is due to very rapid absorption of salt from the intestine after excessive ingestion. This absorption results in a marked increase in the osmotic pressure of the blood and of the cerebrospinal fluid. This in turn causes a movement of water from the interstitial space into the plasma, which causes an increase in its volume and a dehydration of vital tissues, *e.g.* of the brain cells.

(4) *Effect of sodium chloride deprivation.* NaCl deprivation may arise as a result of decreased salt intake in food or due to severe sweating (see p. 216). With sufficient water intake (to compensate for the loss from sweating), a gradual fall in the NaCl level of the blood serum from the normal level of 700 mg/100 cc takes place down to 520 mg. At this point NaCl excretion in the urine ceases; the blood viscosity increases with increased concentration of red cells, plasma proteins and electrolytes generally; complete reabsorption of Cl in the renal tubules occurs; the blood pressure may remain unaltered. The clinical effects of NaCl deficiency are: renal failure (*e.g.* nitrogenous and urea retention in the blood, alkalaemia due to rise of $NaHCO_3$ level of the blood serum, etc.), breathlessness, loss of appetite, mental apathy, muscular cramps (known as *heat cramps*), sense of exhaustion, great fatigue and exhaustion after exertion.

(5) *Influence of CO_2 on chloride shift.* A rise of the CO_2 tension of the whole blood stream (see p. 293) reduces the quantity of plasma chlorides, the chloride of the red blood corpuscles increasing together with the plasma bicar-

bonate. This phenomenon is known as *Chloride shift* or *Hamburger phenomenon.*

(6) *Influence of weather on NaCl excretion.* Daily studies by Tromp in the Netherlands have shown a significant relationship between NaCl excretion and weather. During the passage of active cold fronts and the influx of cold polar air, diuresis, 17-ketosteroid excretion and pH suddenly increase, NaCl excretion decreasing sharply. During warm fronts the reverse is observed. The fact that the hypothalamus, pituitary, adrenal gland and thyroid control the NaCl balance of the body and that these organs are sensitive to weather and climate, makes it clear that the sodium-potassium level of the body must be continually varying as a result of changing meteorological conditions.

Potassium

The amount of potassium excreted per day varies between 2 and 3 g, depending on the food ingested and increasing with a large intake of meat. Potassium ions are intimately related to muscular contraction; KCl injections cause powerful muscular contraction. It is found that the membranes of muscle fibres are permeable to the K ion, but impermeable to Na ions.

Potassium is a very important compound involved in nerve conduction, together with calcium. Relatively small changes in their concentration cause profound changes in the nerve.

Increasing amounts of potassium in the fluids surrounding nerves cause an intitial increase in excitability, followed later by a decrease. A decrease in potassium usually lowers excitability. We have seen (see p. 275) that calcium deficiency has the same effect as an increase in potassium. According to Fenn[188], potassium, together with acetylcholine, also plays an important part in the transmission of impulses from nerves to muscle fibres.

Blood volume

Normally there is a regular relationship between blood volume, body weight and especially surface area, the total volume being made up of the plasma volume and volume of the blood corpuscles. The volume of the blood amounts to 70–100 cc/kg body weight; that of the blood plasma to 40–60 cc/kg; the volume of the blood is 2500–4000 cc/m^2 of body surface, that of the plasma being 1400–2500 cc. Twenty percent of the total blood volume is contained in the two arms and legs, the lungs containing about 1 l. The volumes of both the blood and the plasma are different in people of different ages (volume in relation to weight is below normal in children) and during pregnancy (the volume increases), etc. It depends also on the posture (in an erect posture the volume of the plasma is 15% less than in a horizontal position).

There are a number of factors affecting the blood volume:

(1) *Changes in the total volume of the blood corpuscles* (depending on size and quantity of the corpuscles) and therefore all the factors affecting erythropoiesis (see p. 314).

(2) *Changes in the plasma volume.* The plasma volume itself is kept very constant in a healthy person by adjusting the fluid interchanges between the plasma and the tissue spaces and by controlling the secretion of urine. The plasma volume may be increased temporarily by injecting saline into the body, changing the osmotic pressures. The ingestion of even large amounts of water causes only slight dilution of the blood, as absorption does not take place immediately. In the event of loss of fluid (due to sweating, diarrhoea), fluid is attracted from the tissue spaces because of raised osmotic pressure of the plasma proteins. However, the plasma volume (and, therefore, the total blood volume) may change considerably, due to a number of factors: (*i*) Rise in *plasma protein concentration* causes a decrease in plasma volume and *vice versa.* The lowering of plasma proteins tends to induce new formation of plasma proteins (see p. 286). It may take days for considerabl changes to occur. Pronounced acute changes probably derive from extra vascular reservoirs. (*ii*) Congestive *heart failure* may increase the total blood volume by 20–50%. (*iii*) *Diabetes* with marked ketosis reduces the plasma volume. (*iv*) Traumatic *shock, burns,* severe *intestinal obstruction* bring down the plasma volume. (*v*) Upon the onset of *fever* there is a loss of water from the blood. The blood volume decreases, which favours its withdrawal from the skin to the internal organs and thus reduces the loss of heat. (*vi*) *Adrenal insufficiency* reduces the volume of the plasma (see p. 278). (*vii*) *Hyperthyroidism* (causing active blood supply to muscles for metabolism and to the skin for heat loss) increases the blood volume. (*viii*) *Heat stress* increases the blood volume, *cold stress* decreases it.(*ix*) The blood volume changes with the height of blood pressure and oxygen partial pressure of the atmosphere and therefore changes with *altitude.* Lowered blood pressure causes absorption of fluid from the tissues by the blood, hence increases the blood volume.

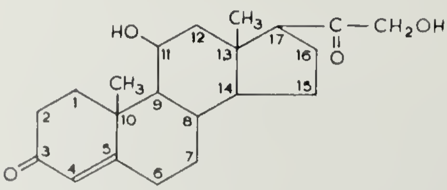
An increase in blood volume may cause an apparent fall in haemoglobin content. The low summer and high winter values (see p. 576) are partly due to actual changes in the haematocrit content of the blood, but in all probability changes in blood volume are partly responsible for them. This is particularly true of rapid changes in Hb values as observed during certain weather changes.

The total protein content of blood also decreases from winter to summer (at least in the Netherlands). Whereas in January 1959 only 40% of blood donors had a protein content of less than 8.0 g/100 cc, in July 1959 this percentage increased to 75. This decrease in plasma proteins in summer increases the plasma volume.

Pulmonary ventilation and various physiological processes related to it depend on the haemoglobin concentration of the blood (see p. 296); hence short and long term fluctuations in blood volume may affect pulmonary ventilation. As some of the changes in blood volume (*e.g.* those created by the adrenal and thyroid gland and environmental changes in temperature and cooling) are related to changing meteorological conditions, we may justifiably assume that abrupt changes in air mass, etc., may well bring about changes in haemoglobin concentration of the blood and their physiological effects.

2. *17-Ketosteroid Secretion*

On p. 278 it was pointed out that the adrenal cortex and testes produce a group of complex organic compounds, the *sterols,* of which the benzine-soluble crystalline compounds are particularly fundamental to various physiological processes of the body. They are known as *17-ketosteroids* (abbr. 17-KS) and were isolated from the urine of males for the first time by Butenandt in 1931. They are characterized by a 4-ring nucleus consisting of a cyclopentane ring attached to a hydrogenated phenanthrene ring system with a ketone group (C=O) in the 17-position and some methyl groups. The presence of this 17-keto group makes it possible to distinguish the various compounds by colour reactions. Here is *corticosterone,* for example:



An excellent summary of these compounds was given by Mason and Engstrom[951] and Lieberman and Teich[949].

A great number of 17-KS compounds are known, the most common ones found in urine under normal circumstances being *androsterone* and *etio-*

cholanolone. Most of these 17-KS originated from the precursor testosterone.

The 17-ketosteroids can influence every phase of metabolism in the body either directly or through their influence on enzyme systems, which accounts for their great importance to a great number of physiological processes.

Factors affecting 17-ketosteroid secretion

(1) *Influence of sex*. The male output exceeds the female after the age of 15 (see below). Average 24 hour secretion in urine of males (according to Hamburger[944]) is 10–15 mg, according to Mason[951] 12.5–16.7 (min. 6.0, max. 25), in females 5–10 mg. In males the 17-ketosteroids originate both from the testes (androgens) and adrenal cortex; in females mainly from the adrenal cortex. Castrated men produce about the same as women. The adrenal cortex production is at its maximum at the age of 20; that of the testes at the age of 30.

(2) *Influence of age*. Studies by Hamburger[944], using 137 males (ages 3-102) and 127 females (ages 2–92), have given the following results: (*i*) The output of 17-KS rises abruptly both in males and females during puberty and adolescence, reaching a maximum at the age of 25 (15 mg in males and 10 mg. in females per 24 hours). (*ii*) With growing age the production falls gradually; in females there is an abrupt fall from 25 to 35, after which point the production remains fairly constant up to the ages of 50 and 60, followed by a gradual fall. (*iii*) Up to the age of 15 the rise in output of boys and girls is the same; from then on the male output is higher.

TABLE 29

AVERAGE AMOUNT OF 17-KETOSTEROID SECRETION IN MG/24 HOURS

According to Hamburger[944]			*According to Zimmermann*[960]		
age	*males*	*females*	*age*	*males*	*females*
0–10	2	2	5	2	2
10–20	11	8	10	5	5
25	15	10	15	9	9
30	14	8	20	13	12
35	—	6	25	17.5	12.5
40	12	6	30	16	11
50	11	6	35	14	9
55	—	6	40	12.5	7.5
60	7.5	4.7	45	11	7
70	5	3.5	50	9	6
80	4.5	2	55	7.5	5
			60	7	5
			65	5	4
			70	5	4
			75	4	4

(3) *Influence of race or diet.* Studies by Lugg and Bowness[950], Awad[934], Friedman[942], Barnicot[936] and others show the following average 17-KS values for healthy males between 20 and 40: Malayans 8 (max. 15), Egyptians 9 (max. 15), Chinese 9 (max. 17.5), Indians 10 (max. 14), Europeans living in India 21, Mexicans 7, African Negroes 8 (max. 12), American Negroes 15–16 (max. 25), Whites in U.S.A. and Europe 15–16 mg (max. 25). The difference between African and American Negroes makes it look as though sociological, dietary or climatological rather than racial differences (see later) are responsible for the observed difference. This is supported by the following observation: It is known that a shortage of proteins in the diet reduces the resistance of the body, perhaps partly on account of reduced formation of gamma globulin, a plasma protein concerned with the phenomena of immunity. Along with this goes a decrease in 17-KS secretion. Serious protein deficiency (in excessive carbohydrate diets) may reduce the 17-KS secretion by 30%.

(4) *Bronchial asthma.* Hioco and Samter[946], comparing 10 healthy persons with 22 patients suffering from bronchial asthma, were unable to discover significant differences in 17-KS secretion between the two groups. They did, however, notice that there was less secretion of 11-oxycorticosteroid during severe asthma attacks (normal production 1.1–1.6 mg) and more of 11-desoxycorticosteroid (normal production 0.15–0.25 mg). Eriksson-Lihr (in 1949) likewise found normal values. Venning and Rose (in 1951), on the other hand, found definitely less excretion of 17-KS in association with bronchial asthma. Israels *et al.*[947], studying 80 asthmatics (44 women, 36 men) as compared with 66 normal (42 women and 24 men), noted that up to 40 years of age the excretion of 17-KS was significantly lower than in the control group; within the group women between 40 and 50 there was no significant difference; asthmatic women of over 50 excreted a higher amount than normal women. It was also found that in asthmatic patients with a purulent bacterial bronchitis 17-KS secretion is significantly higher than in the non-infected patients, probably due to a continuous stress condition.

(5) *Influence of exogenous hormones.* The administration of testosterone increases 17-KS secretion; 17-methyl testosterone or oestrogens cause a decrease; progesterone seems to have little or no effect. ACTH stimulates excretion. The influence of the thyroid is demonstrated in myxoedema (see p. 268), the amount of 17-KS secretion being very low (it may be even less than 2 mg). A slight decrease is also noted during hyperthyroidism. In association with controlled diabetes mellitus a decrease was observed. Dysfunction of the liver causes decreased 17-KS secretion; in infectious hepatitis the amount may even be very small. Spondyl- or rheumatoid

arthritis may cause a considerable increase, up to 27 mg/day. This is a very important observation, because *cortisone* (17-hydroxy-11-dehydrocorticosterone) has temporary favourable effects on these rheumatic diseases. Considering the great effect of weather and heat regulation capacity of the body on 17-KS secretion (see below), this observation may give us a valuable clue to the possible influence of weather on certain forms of rheumatic diseases. It is an interesting fact that gout may greatly reduce 17-KS secretion to values as low as 3 mg.

(6) *Influence of diuresis.* The volume of urine secreted has little or no effect on 17-KS secretion.

(7) *Daily rhythm.* According to Pincus the rate of excretion during the day is 30–50% greater than during the night. The maximum excretion is in the morning. According to Zimmermann[960], the maximum is at about 2 p.m., the minimum at night.

(8) *Stress.* (*i*) Under conditions of extreme unpleasant *mental stress* or excessive exercise and fatigue a sharp increase in 17-KS secretion can be observed. Daily studies by Tromp at Leyden during 1959 and 1960, however, revealed little or no effect of normal daily mental stress conditions or *sexual activity* in males. According to various authors, decreased 17-KS secretion may ensue from permanent hypertension. (*ii*) The influence of changing *meteorological conditions* on 17-KS secretion was demonstrated for the first time by Zimmermann *et al.*[1304] in 1951 (Fig. 51) in the Endo-

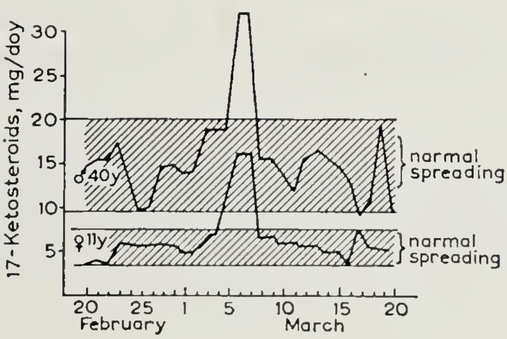


Fig. 51.
Influence of meteorological stress on 17-ketosteroid secretion of a 40 years old male and an 11 years old female at Trier (Germany) (after Zimmerman *et al.*[1304]).

crinological Institute at Trier (Germany). A healthy man of 40 and a girl of 11 were observed for 4 weeks. Both male and female showed the same sharp increase (up to 290%) on special föhn days. This suggested that probably only the adrenal cortex was affected and not the man's testes.

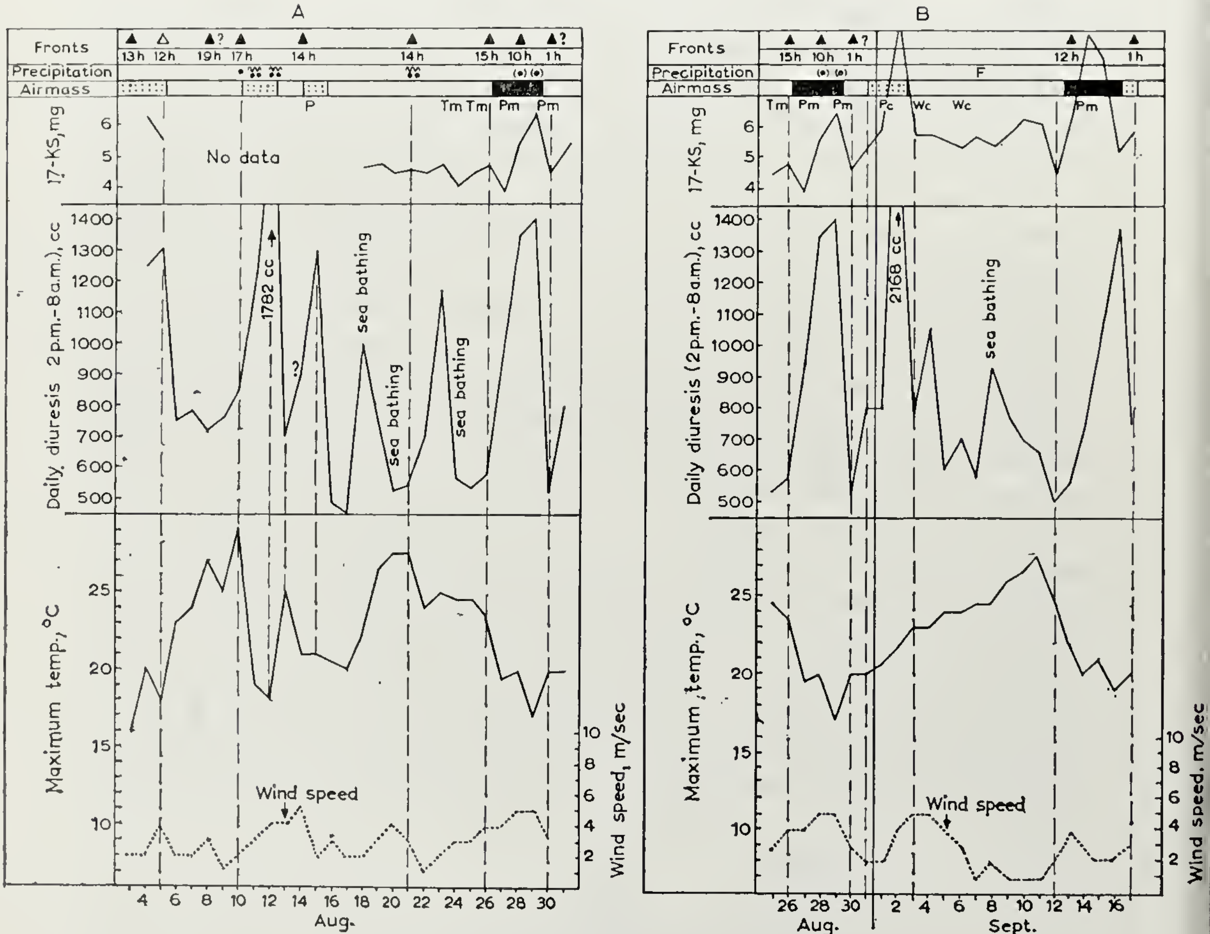


Fig. 52.

Daily diuresis and 17-ketosteroid secretion in a healthy male subject at Leyden (The Netherlands), as a function of temperature, airmasses and weather fronts. A: period 3–31 August 1959; B: period August 25th-September 17th, 1959. ●: rain; (●) : slight rain; ⁓ : lightning; ▲ : cold front; △ : warm front; ■ : polar air, cold; □ : tropical maritime or warm continental air; ▭: polar air heated over Atlantic Ocean or continental air of medium temperature; F: fog; Tm: tropical maritime; Pm: polar maritime; Pc: polar continental; Wc: warm continental (after Tromp).

Daily observations by Tromp (Fig. 52) on the same healthy male during a period of 2 years (1959–1960) confirmed these findings. A steep rise in 17-KS secretion is observed (in W. Europe) during or shortly after the influx of cold polair air masses or active cold fronts, particularly if the influx is preceded by a warm period with little atmospheric turbulence. The increase in 17-KS secretion may exceed the pre-frontal values by 100% or more. After the influx of warm air masses or warm fronts the secretion decreases. However, relatively high 17-KS values are found if temperatures and humidity are very high and reach a point affecting human comfort (see p. 230). The rise in the KS production more or less coincides with increased diuresis (see below) during a steep drop in environmental temperature, but it may precede the rise in diuresis by 24 hours or more. In other words, as stated above, there is no direct relationship between 17-KS secretion and urinary volume. In mental patients (particularly schizophrenics) the meteorotropic effect may be opposite to the one observed in normal man, *i.e.* a decrease in 17-KS secretion during cold stress.

(9) *Influence of radiation.* Studies by Myerson and Neustadt[1113] indicate an increased 17-KS secretion (almost doubled) after a short period of U.V.-radiation, which may be reduced again if the U.V.-intensity becomes too strong. Zimmermann[962] thinks that this may account for the observation made by Rollier and others that U.V. solar radiation, if weak, increases resistance to tuberculosis; the resistance is feeble if the U.V.-intensity increases above a certain level.

(10) *Influence of altitude.* In 1954, Koller, Schwarz and Marti observed in 8 persons, moved from Zurich to Davos (difference in altitude 1150 m) an increased 17-KS secretion, together with an increased leucocyte and thrombocyte count and a decrease in eosinophils. Burril and Ivy (in 1950) found the same in low pressure chambers.

This brief summary of the main characteristics of these very important organic compounds may account sufficiently for the pronounced influence of weather and climate on various physiological functions. External changes in environmental temperature and cooling are recorded by the hypothalamus-pituitary-adrenal system and the stimulus is reflected in changing 17-KS levels of the blood and urine which may affect various phases of metabolism in the human body. Zimmermann's work suggests that these changing ketosteroid levels are also closely involved in balneological effects[960] and in the general resistance of the body to infectious diseases[961].

Possible relationship between 17-ketosteroid level and resistance to infectious diseases.

Zimmermann distinguished between two types of physiological reisistance to infectious diseases: (*i*) Resistance to the penetration of viruses or micro-organisms into the body; (*ii*) Resistance enabling the body to destroy the pathogenic effects created by micro-organisms which have succeeded in entering the body.

For many years Zimmermann studied the possible relationship between general resistance and the 17-KS level. He noticed repeatedly a marked decrease in excretion of the 17-KS shortly before the outbreak of an infectious disease. The time lag coincided with the incubation period. Moreover, the general 17-KS level accompanying various diseases seems to be very low when the resistance to infectious diseases is low, and *vice versa*. Zimmermann gave the following examples: The 17-KS produced is found to be depressed during various hormonal diseases (*e.g.* Addison's disease, diabetes, hypothyroidism), the general resistance to infectious diseases being low; babies, young children and old people produce little 17-KS secretion, their resistance to infectious diseases being low; protein and vitamin deficiency in diet reduces both 17-KS secretion and general resistance. Normal bodily exercise increases resistance and 17-KS secretion; excessive exercise lowers both; serious operations lower 17-KS secretion and resistance to infection. According to Zimmermann, the high incidence of tuberculosis in many tropical underdeveloped areas may be at least partly related to the low 17-KS values in these areas (see above).

It is fully realized that these relationships do not have to be causal, but Zimmermann noticed repeatedly, in individual patients as well, that the 17-KS value reached a minimum a few days before the onset of pneumonia, an ordinary cold, influenza and so forth. The properdin level of the blood (see p. 315) shows the same fluctuations. Zimmermann explains this action of 17-KS as an *anabolic property* of these hormones, *i.e.* a constructive process in protein metabolism, particularly in the cells of the reticulo-endothelial system (see p. 284).

Influence of 17-ketosteroids on balneological effects

Several authors have reported increased 17-KS secretion after sulphur baths, thermal baths, sauna baths (in Finland), etc. Most studies, however, lack the further evidence which only experiments, carried out for a longer period, can furnish. The many factors affecting 17-KS secretion make it necessary to study the same patient for a very long time before a definite conclusion can be drawn.

3. *Diuresis*

The amount of urine excreted is very closely related to the environmental meteorological conditions; in fact, it is probably one of the most sensitive of biometeorological thermometers (see p. 40). Apart from the influence of environmental temperature, humidity and wind speed (*i.e.* the cooling effect) and the amount of fluid consumed, diuresis is controlled by the adrenal cortex, the pituitary and the hypothalamus (see p. 203). However, as the two *kidneys* are a vital element in this whole process, a brief anatomical description should be given of this important organ.

Structure of the kidney

It consists of about one million small units, the *nephrons*, which drain fluids via collecting tubules into the renal pelvis and finally into the ureter. Each nephron consists of two parts: (*i*) *Bowman's capsule*. This is intruded by a group of capillary vessels, the glomerulus. Capsule and glomerulus form together the Malpighian (or renal) corpuscle, the main function of which is to filter out a cell free fluid from the blood, identical to plasma except for proteins and colloids which do not pass through. (*ii*) The *renal tubule proper*. This consists of 3 segments, the proximal, the distal and the collecting tubule.

Blood and nerve supply

The kidneys have an enormous blood supply (approx. 1300 cc/min in man), which is assisted by a double capillary network, the glomeruli and capillaries on the surface of the renal tubules. The level of blood pressure (depending on cardiac output and calibre of the renal arterioles and capillaries) is of great importance for the functioning of the kidneys and its filtration mechanism. If the blood supply decreases an enzyme, *renin*, is discharged into the circulation. With the normal plasma euglobilin, hypertensinogen, a blood pressor agent is formed known as *hypertensin*.

Orthosympathetic motor fibres do not affect the nephrons directly, but affect the kidney by changing the local blood flow.

Functions of the kidney

It keeps the plasma volume (see p. 323) and water content of the body as a whole fairly constant; it helps to preserve the pH of the blood (see p. 292); it eliminates waste products derived from protein metabolism and from tissue cells (particularly nitrogenous and sulphur-containing compounds) it regulat esosmotic relations in the blood (see also p. 204); it assists in regulating the sodium-potassium balance; it eliminates toxic substances.

Mechanism of renal excretion and reabsorption

In the glomeruli, with relatively high blood pressure, each minute 120 cc of fluid are filtered off from 700 cc of plasma and passed into Bowman's capsule. The ratio 120/700 is known as filtration fraction. The total filtrate in 24 hours is about 170 litres.

The glomerular blood pressure (*ca.* 75 mm Hg) drives fluid out of the blood vessels into the capsule, but this process is opposed by the osmotic pressure of the plasma proteins (roughly 25 mm Hg). This difference in pressure determines the volume of the glomerular filtrate. With increasing blood pressure (*e.g.* due to cold or mental stress) the filtrate volume may increase considerably. This volume depends also on the physical properties of the filtering membranes.

The *permeability* of the glomerular endothelium and of the capsular epithelium is increased in presence of anoxia, toxic substances, etc. (see also p. 288). Normally the membranes prevent the filtering of globulins or albumins (6–7 $\mu\mu$). Molecules $\leqq 4\ \mu\mu$ can pass, but increased permeability (see p. 335) allows albumin to escape, causing *albuminuria*; at a later stage, globulins escape and finally even blood cells.

The fluids which passed the glomeruli can be reabsorbed in the renal tubules and brought back into the blood. This specific reabsorption, depending on the bodily needs, is controlled by a number of factors which are only partly known:

(1) *Water reabsorption.* (*i*) *Anti-diuretic hormone.* On pp. 203 and 259 we pointed out that a dense network of axons of the anterior nuclei of the hypothalamus pass down along the pituitary stalk into the posterior lobe of the pituitary, affecting the secretion of vasopressin which reaches the kidneys through the blood stream. It stimulates the renal tubules, causing reabsorption of water. Not only the posterior lobe, but also the anterior lobe seems to affect diuresis, although in an indirect manner. The removal of the anterior lobe reduces water intake; anterior lobe-extracts produce polyuria and thirst. (*ii*) *Adreno-cortical hormones.* As stated on p. 278, they increase the absorption of NaCl in the proximal renal tubules and therefore impair the antidiuretic hormone activities. In other words, they promote urinary excretion. The effect of adrenal dysfunction was described on p. 278. It emerged from recent studies by Itoh *et al.*[948] in Japan that, whereas normally cold stress increases urinary secretion (see below), adrenalectomy or hypophysectomy prevents this cold-stress effect*. (*iii*) *Thyroid hormones.* The evidence of studies by Itoh *et al.*[948] is that thyroidectomy increases water excretion. Although the thyroid hormone may affect diuresis indirectly through its influence on the adrenal gland (see p. 279), Itoh's experiments suggest that the thyroid hormone has no direct effect on the renal function. Still a number of observations point to the influence of the thyroid on diuresis: we mentioned briefly (see p. 202) that interruption of the pathways

* The influence of the adrenal cortex on diuresis is used to determine adrenocortical insufficiency: Kepler, Soffer and Gabrilove test[748], Oleesky test [723] and Cutler-Power-Wilder test[606].

from the supra-optic nuclei of the hypothalamus to the pituitary may cause excessive urinary flow known as *diabetes insipidus*. Thyroidectomy cuts down the urinary flow. If afterwards thyroid extract is administered, urinary flow increases again enormously. The observation that thyroid extracts have a diuretic action in normal subjects and the diminished flow observed in myxoedema (see p. 268) also go to show that the thyroid affects renal excretion considerably, though probably not directly. (*iv*) *Parathyroid hormone*. As stated on p. 275, hypercalcaemia may induce increased urea and nitrogenous products in the blood due to renal failure.

(2) *Glucose reabsorption*. This is brought to a complete standstill by phloridzin, cyanide, etc. As a result of hyperglycaemia, the glucose in diabetes mellitus patients (see p. 259) is not completely reabsorbed by the tubules. The sugar content of the urine increases. The severe osmotic pressure created by this high sugar concentration hampers the absorption of the normal quantities of water and results in polyuria.

Other factors affecting the urinary volume: Salt ingestion and protein intake increase diuresis; the same is true of diuretic agents in food (*e.g.* caffeine); muscular excercise reduces diuresis; sleep reduces urinary output; emotion may inhibit or increase urinary flow. As indicated above, all factors increasing the blood pressure may increase urinary flow.

Effect of drinking water

After deprivation of water, a craving for liquid is created *(thirst)*, probably as a result of various physiological changes. According to Cannon, dryness in the mouth is due to reduced salivation*, followed by greater dryness of inhaled air passing the pharynx; the expired air becomes dry and warm. After drinking water, absorption takes place rapidly from the intestine. The passage of water into the blood causes dilution of the plasma and there ensues a fall in osmotic pressure; the plasma volume increases slightly. The excess fluid is stored rapidly in the tissue space. After 15–30 minutes the kidneys become active; the flow of urine augments. As the volume increases, its specific gravity declines. The increased thirst, observed by healthy people during very dry and cold weather, particularly if accompanied by strong wind, is probably due to dryness of mouth and pharynx, increased evaporation of the insensible perspiration on the skin and increased urinary flow.

Influence of meteorological factors

(1) *Influence of temperature*. As described above, and in previous sections

* Atropine (orthosympathetic stimulation) checks salivation and gives rise to thirst; pilocarpine (parasympathetic stimulation) releaves it, according to Pack *(Amer. J. Phys.* 65, 346, (1923).

on thermoregulation, sudden changes in temperature, particularly those accompanied by air movement, are immediately recorded by the hypothalamic-pituitary-renal system. Appreciable loss of water through excessive perspiration is counteracted by the mechanisms described. Observations made by Tromp in the Netherlands on 540 consecutive days in 1959 and 1960 upon the same healthy adult male (age 50 years) have clearly demonstrated the following relationships (Fig. 52): (*i*) During influx of cold polar air or after the passage of active cold fronts, diuresis increases steeply; after warm fronts or the influx of warm tropical air, it declines sharply. (*ii*) Sudden local changes in temperature, particularly during the day, are also reflected in the increase and decrease of diuresis. (*iii*) This phenomenon is in evidence in persons out of doors for an hour or even less; but even indoors the influence of drastic changes in meteorological conditions is often recorded by the human body (see p. 82) and is reflected in the daily diuresis. (*iv*) Sea-bathing, even in summer, is usually followed by a marked aggravation of diuresis. (*v*) Increased diuresis usually coincides with, or follows, increased 17-KS secretion. (*vi*) In mental patients, particularly schizophrenics, an entirely different picture was observed. Often a steep fall in diuresis takes place during influx of cold polar air and a rise during influx of warm air masses.

Whereas the amount of water consumed and several other factors mentioned above affect the total amount of urine excreted, the daily diuresis curve of a normal healthy person, provided the fluctuations exceed several hundred cc, has proved to be an excellent indicator of biometeorological temperature, which is of great value to the study of other meteorotropic phenomena.

(2) *Influence of radiation.* As indicated on p. 266, U.V.-radiation affects the function of the pituitary, the adrenal cortex and 17-KS secretion. As adrenal cortical hormones affect renal function (see above), changes in U.V.-radiation may also considerably affect the amount of daily diuresis.

(3) *Influence of atmospheric pressure.* Various experiments have been described (see p. 298) which demonstrate the influence of decreasing atmospheric pressure (by 3–9 cm Hg) on water retention. This may be at least partly due to adrenaline secretion causing a diminished total renal blood flow and a constriction of the glomerular efferent arterioles of the kidney. This in its turn causes a more complete reabsorption of water from the tubules, into the blood.

4. *Capillary Resistance and Permeability of Membranes*

The influence of the adrenal gland and pituitary on capillary resistance and permeability was described on p. 280, the active principles being corticosteroids and the growth hormone. The former group and adrenaline increase the resistance, whereas the growth hormone and pilocarpine tend to decrease it. On the same page we referred briefly to the interesting studies on the influence of altitude and foehn, made by Regli and Stämpfli[1378], which were carried out in Switzerland in 1947, and of which we give a more extensive review below.

Influence of altitude

Healthy people moving from Lauterbrunnen to the Jungfrau Joch (over 4000 m high) displayed increased capillary resistance. The same was observed in asthmatic patients moving from Zürich to the Upper Engadine, the increased resistance coinciding with an improved condition of the asthmatics. It is relevant here to mention the significant fact that Wyss and Gianoli[1379] observed a decrease in capillary resistance during attacks of bronchial asthma. As increase in altitude stimulates the adrenal gland and increases adrenaline secretion (see p. 294) the effects described might be due entirely to both increased orthosympathetic stimulation and adrenal functioning.

Influence of foehn

The origin of this warm wind, prevailing in many mountain valleys in Switzerland, was discussed on p. 24. Regli carried out his studies in a valley near Erstfeld (Kanton Uri), which is particularly notorious for the prevalence of the foehn. The capillary resistance of 37 children and 3 adults was studied for 47 days. On the basis of 1600 observations the following results were obtained: (*i*) During periods of high atmospheric pressure the capillary resistance (C.R.) fluctuations were small. These values were taken as the norm. (*ii*) After the passage of warm fronts the C.R. was observed to decline, while after cold fronts it increased. (*iii*) Shortly before the foehn wind reaches the valley the C.R. is found to rise and usually decreases again slightly after the foehn air mass has penetrated into the valley. (*iv*) Changes, usually pronounced, in the C.R. are observed in people, suffering from subjective complaints during a foehn. The reverse, however, is not always true. Some people with greatly fluctuating C.R. are not sensitive to the foehn.

Regli and Stämpfli's observations of the influence of cold and warm fronts were confirmed by Lotmar and Häfelin[1376] in 1955 and by Arimatsu[1377] in Japan in 1957.

Physiological effects of changes in permeability

The *weather-controlled decrease in capillary resistance, or increase in* *permeability,* has several important physiological effects, *viz.,* (*i*) It may facilitate the penetration of micro-organisms or viruses (and the toxic substances created by them) and of other toxic substances through the skin, mucous membrane of the nose, etc. (*ii*) As was stated on p. 297 owing to a difference of about 55 mm Hg between the arterial blood and resting tissue, oxygen can pass rapidly out of the blood plasma through the capillary wall and tissue into the tissue cells. With increased permeability of the membranes the process is accelerated. In other words, it favours oxygen intake and CO_2 release. (*iii*) Increased permeability of the glomerular endothelium and of the capsular epithelium affects renal function, as explained on p. 332. (*iv*). Various important biochemical processes in the stomach and intestines are affected by changing permeability of the various membranes.

These few examples may explain sufficiently the significance of the in fluence of meteorological changes on permeability in a number of vital physiological processes. The influence of solar radiation on various physiological processes has been mentioned briefly in a number of preceding sections. The following section, prepared by Dr. F. P. Ellinger, will provide a more systematic survey of the major biometeorological radiation penomena.

Subsect. I. INFLUENCE OF SOLAR RADIATION ON HEALTH AND DISEASE

1. General Principles

by

F. P. ELLINGER

Among the various factors contributing to the climate of man, the importance of the sun has been recognized as essential to health since time immemorial. The Father of Medicine, the Greek physician Hippocrates (460–377 B.C.)[1011], outlined the ancient point of view as follows: "Those cities which are located in the direction of the rising sun are healthier than those located in the North or those exposed to hot winds . . . First of all, the effect of heat and cold is moderated in these cities. Furthermore, in a city with an eastern location the water is—by necessity—clear, well smelling and tasty, because the rising sun prevents, through its rays, spoiling of the water. As concerns the complexion of the people, they look healthy and have a pleasant skin color, unless being sick." Recognition of the importance of sunlight for the wholesomeness of water as the basis of human well-being expressed in this quotation from Hippocrates found its scientific verification through the work of Downes and Blunt[982], who established in 1877 the bactericidal (bacteria killing) action of sunlight and linked this effect to the self-purification of rivers and lakes exposed to sunlight. Later investigators (particularly Bang [963], Bie [966] and Busk[971]) indicated that it is the ultraviolet content of the sunlight which is responsible for this effect*.

The other aspects of the influence of sunlight on health, mentioned by Hippocrates, the pleasant skin color of inhabitants of locations with a favorable radiation climate, represents an experience which holds good up to the present time. In the general opinion, a "sunburned" skin, *i.e.* a skin on which exposure to the sun has either produced a pinkish color (skin erythema, or photoerythema, in scientific language), or the so-called "suntan" (a skin pigmentation or photopigmentation), is considered a sign of good health**.

The phenomenon of "sunburn" has stimulated a host of investigations concerned with its etiology (causation) and mechanisms. Through the work of Hammer[1002] in 1891, it was indicated that "sunburn", *i.e.* the erythema of the skin which develops usually within 4 to 7 hours after exposure to sunlight, in all probability, is not the result of heat-producing rays (red and infrared rays with wavelengths from 7600 to 10,000,000 Å), but rather is due to invisible rays emitted by the sun, the so-called ultraviolet rays (wavelengths 4000 to 1200 Å). During the years 1893–1896, the Danish physician, Niels Ryberg Finsen (1860–1904), in a series of now classical experiments[996], [997], established beyond doubt the importance of the ultraviolet content of sunlight as the essential causative agent of sunburn and of the healthful effects of sunlight on the human body. Finsen thus became the father of modern photobiology and its application to the cure of diseases by sunlight, the so-called heliotherapy (also known as light-, sun-, or ultraviolet therapy).

The importance of sun-ultraviolet was emphasized further through the incidental discovery of the antirachitic action of ultraviolet rays by the German pediatrician, K. Huldschinsky[1015] in 1919. This observation lead eventually to the discovery of photochemical*** formation of vitamin D from ergosterol by these rays.

Establishment of the importance of sun-ultraviolet for the health of the

* There exists a host of investigations on the germ-killing action of ultraviolet which is chiefly confined to the region between 3287 and 2265 Å. For details see Laurens[1025], Ellis and Wells[992], Hollaender[1012, 1013] and Ellinger[987].

** This, however, has not been verified by later scientific investigation. At best, it can be considered as a coincidence (see Ellinger[987, p. 625]).

*** For details concerning vitamin D formation by ultraviolet light and also formation of other biologically important chemical compounds by these rays, see Ellinger[987], chapter 3 human race has stimulated a host of investigations concerned with quantitative and qualitative aspects of this part of the solar spectrum. As a result of these, we have at our disposal pertinent data from all parts of the world* which form the body of that branch of physical sciences called *radiation climatology*.

From the accumulated evidence (see also p. 22) it appears that the sun-ultraviolet content on our earth varies quantitatively and qualitatively due to geographical location, altitude above sea level, season and time of day, and that there are further modifying factors such as cloud-formation, dust accumulations (see special studies on big cities), geological formations, and snow-layers (Hausmann, Kuen[1008]) or sand dunes (Büttner, Sutter[974]). As will be shown later (see page 339), not all ultraviolet rays are equally biologically effective. These modifying factors are, therefore, of great importance in assaying the potential effect of sun-ultraviolet under specified conditions. Under the most favorable conditions the shortest wavelength measured was that of 2900 Å[1061], and the greatest variations in intensity of erythema-producing rays may amount to 1 : 3 (Knudson[1022]).

2. *Biological Effects of Ultraviolet Radiation*

by

F. P. ELLINGER

Local effects on the human body

Since Finsen's classical studies revealed the pre-eminence of the ultraviolet radiation of sunlight for its biological effectiveness, we shall start our more detailed description of the biological effects of sunlight with this part of the spectrum.

(1) *Effects on the human skin.* As the result of exposure of human skin to sunlight, the following biological phenomena are observed: Development of a reddening of the skin (due to increase of blood flow) the so-called *photoerythema*. Characteristic of this phenomenon is that it does not occur instantaneously, but that it appears after a certain amount of time has elapsed, a so-called "latent period". The length of the latent period is reversely propor-

* Abyssinia[1041], Albany, N.Y. (USA)[1021], fourteen cities in USA[1016], Assuan (Egypt)[1023, 1050], Baltimore, Md. (USA)[975], Buenos Aires (Argentina)[1052], China[1058], Cleveland, Ohio (USA)[1032], England[1010], Flagstaff, Arizona (USA)[978], Greifswald (Germany)[964], Hallstatt (Austria)[1042], Honolulu, Hawaii (USA)[999], Jamnagar (India)[1041], Kanzelhöhe, Carinthia (Austria)[983], Munich (Germany)[1033], New Orleans, La. (USA)[1034], Prague (Czechoslovakia)[1047], Rheinebene (Germany)[1045], Riesengebirge (Germany)[1001], Switzerland[1040], Tropics[976, 1043, 1051], Thüringerwald (Germany)[968], Washington, D.C. (USA)[978, 977], Vienna (Austria)[1008, 1027]. Special studies on radiation climatology of big cities: Berlin[973], Wroclaw[1000], general studies [1036, 1037]. Radiation climate of rooms[1038]. General biology of radiation climate[1057, 1014].

tional to the intensity of the radiation and may be as short as 1 hour at high intensities. Exposure to moderate intensities, as they prevail at sea level, produces a photoerythema with a latent period from 4 to 7 hours usually. The photoerythema increases in intensity and usually subsides within 18 to 24 hours. As the erythema starts to fade, the skin acquires a brownish colouration, a phenomenon designated as *photopigmentation,* which may last for months or even years. The colour is due to oxidation of the *melanin* pigment in the epidermis of the skin. The corneum is thickened. Both processes reduce the effect of further irradiation.

If exposure to sunlight takes place at higher intensities, as they prevail in high altitudes*, or in the course of excessive sunbathing, the result is a painful reddening of the skin with swelling (edema), a phenomenon which is called a *second degree* reaction. Still more intensive exposure to sun-ultraviolet may lead to the formation of fluid-containing blisters, the so-called *third degree* skin reaction. If no infection of these blisters takes place they heal without sequelae. Second or third degree skin reactions are usually also followed by pigmentation, which, however, is more intense.

As the result of irradiation with sun-ultraviolet, a dilation of the smallest blood vessels of the skin, the skin capillaries, takes place, which accounts for the phenomenon of photoerythema. At the same time a progressive pigment migration to the uppermost layers of the skin, the cornified skin layer (stratum corneum), takes place. This is due to the development of dendritic cells into which the pigment is transferred from its original location somewhat deeper in the skin (stratum pigmentosum) by intracellular deposition. Besides this pigmentation, subsequent to the production of an erythema (*secondary tanning effect*), there exists also a *direct* tanning effect due to an increase in pigment granules in the basal cells of the skin, as demonstrated by Hamperl *et al.*[1003] in 1939.

* Note by S. W. Tromp: In biometeorological studies the ultraviolet spectrum is usually clasified into three groups: *ultraviolet A* (wavelength 400-320 mμ), *ultraviolet B* (also known as *Dornoradiation,* wavelength 320-290 m μ, of which the wave interval 302-297 m μ is particularly important as anti-ricketsagent) and *ultraviolet C* (wavelength less than 290 m μ). At high altitude the intensity of U.V. radiation is about 30% larger than at sealevel. Holtz[504] pointed out that the actual cause of pronounced physiological effects, often observed in tourists spending their holiday at 2000 m altitude, may be a different one.

A few hours after a long exposure to sunlight at this altitude the following observations can often be made in healthy people: loss of appetite, nausea, fatigue, headache, fever, insomnia, etc. This is not observed if the tourist would stay indoors at this altitude.

At 2000-3000 m altitude even wavelengths of 278 m μ may reach us. At sea level, during several months of the year, wavelengths of 300 m μ may not penetrate to the earth surface due to atmospheric absorption. As the absorption curve of U.V. for many proteins increases sharply below 295 m μ, this may be one of the reasons of the observed intoxication phenomena apart from the effect of U.V. on pituitary, thyroid and adrenal (see pages 261 and 272).

A further result of exposure of the skin consists in an *increased cornification* This represents a compensatory hypertrophy of the skin similar to that seen after mechanical skin irritation and well known as "callus" formation.

Increased skin cornification, together with pigment formation, accounts for the phenomenon of *photoadaptation,* a condition in which the skin is rendered more resistant to sun-ultraviolet, *i.e.,* a second exposure to the same or even higher intensity than the one which produced these phenomena, is tolerated without notable erythemic response.

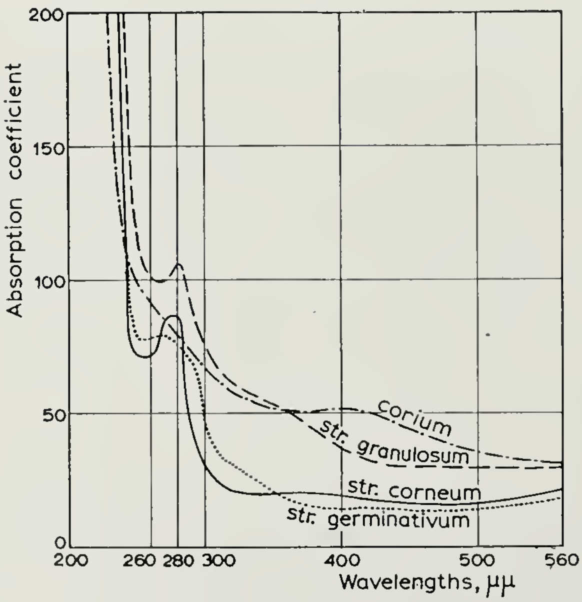


Fig. 53.
Light absorption of various skin layers (after Bachem) (according to Ellinger[987]).

Hausser and Vahle[1009] in 1921 started a series of experiments in which they demonstrated that not all ultraviolet rays were equally effective in producing erythema and pigmentation. They established a definite action spectrum for photoerythema. Their observations were confirmed in other quarters (for details see Ellinger[987]). From the accumulated evidence, it appears that there exist two maxima for the erythemic response of the human skin; a first one at the wavelength of 3800 Å and a second one between 3030 and 2970 Å. A specific absorption of these rays in the skin has been recognized as the reason for this specific action (for details see Ellinger[987]) (see Fig. 53). With regard to pigmentation, Peemöller[1044] pointed out that ultraviolet with longer wavelengths was more effective than that of shorter wavelengths. It is for this reason that antisunburn media which filter the shorter wavelengths out and, in this manner, prevent painful erythemic responses, permit nevertheless suntanning (photopigmentation).

Since the action spectrum of vitamin D formation differs from that of photoerythema, this biological phenomenon cannot be used unreservedly for assessment of the antirachitic power of ultraviolet (for details see Ellinger[988]).

The action mechanisms of ultraviolet radiation on the skin consist in the formation of vitamin D from ergosterol, in the photochemical formation of histamine from the amino acid histidine, and/or release of pre-existing histamine from ultraviolet-damaged skin cells (for details see Ellinger[987]). According to a theory advanced by Rothman[1054] in 1946, destruction of an inhibitor of the enzymatic process preventing melanin formation in the tyrosine-tyrosinase system could explain the direct as well as the indirect effects of suntanning (for details see Ellinger[987]).

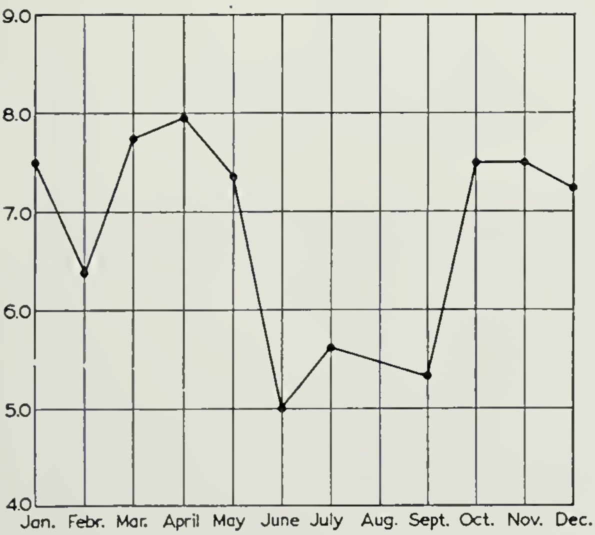


Fig. 54.
Photosensitivity of the human skin with changing season (according to Ellinger[987]).

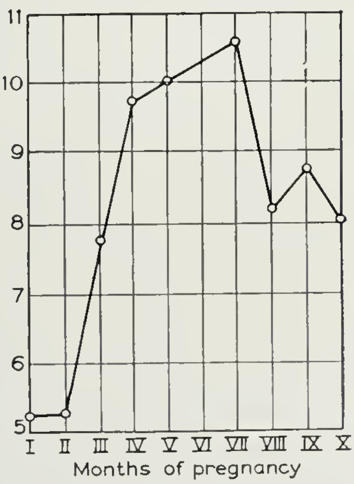


Fig. 55.
Photosensitivity during the months of pregnancy (according to Ellinger[987]).

The response of human skin to a given part of the sun spectrum is called *photosensitivity*, which varies not only with the change in the spectrum, but also with physiological and pathological conditions of the human body. Fundamental studies in this field have been performed by Busk[972], Schall and Alius[1056], Saidman[1055], Wucherpfennig[1066], and Ellinger[991, 989]. From the accumulated evidence it appears that the following factors determine photosensitivity: (*i*) *Color of the hair, age of the individual, sex and season.*

Blond persons, and particularly red-blondes, are, in general, more photosensitive than persons with dark hair. Young children are less photosensitive than adults (age range 20 to 50 years). During the involutionary period of life photosensitivity declines. Males appear more photosensitive than females. Finally, the photosensitivity is higher in spring and early fall than in winter and summer (Fig. 54). (*ii*) *The body section.* Photosensitivity decreases in the order: breast - abdomen - back - cheeks - upper and lower extremities. (*iii*) *Constitutional factors.* The following factors have been recognized as influencing photosensitivity which is increased during the first days of the menstrual cycle of women and also during pregnancy[986] (see Fig. 55). The constitutional type of vegetative stigmatization exhibits increased photosensitivity the year-round* (see Fig. 56).

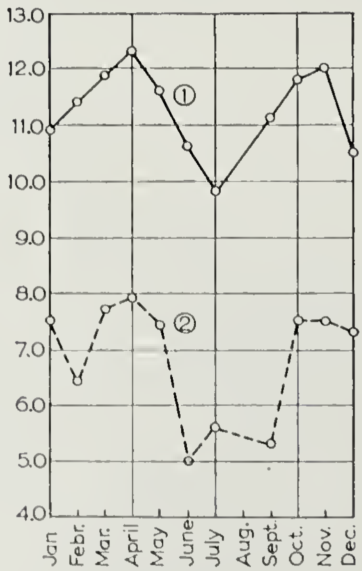


Fig. 56.
Photosensitivity in sympathicotonic individuals (according to Ellinger[987]). 1: Monthly fluctuation in sensitivity of sympathicotonic cases between 20–50 years; 2: combined curve of all adults between 20–50 years.

(2) *Effects on the hair.* The bleaching effect of sunlight is a matter of common knowledge, which may be accompanied by damage to the hair cuticula (Friedrich[998]).

(3) *Effects on the eye.* As a result of exposure of the eye to ultraviolet radiation, more or less severe inflammation of the eyelids and conjunctivae

* For details and relationship to the pathophysiology of gastroduodenal ulcers, see Ellinger[999].

may occur. These symptoms may be very painful, but usually clear up without serious sequelae. The role of ultraviolet radiation in the formation of cataracts is disputed (for details see Ellinger[987]).

General effects on the human body

As the result of exposure of human skin to sun-ultraviolet producing an erythemic response, a number of effects inside the body have been observed. Since these rays have a very low penetration power only, these effects must be considered as indirectly produced. Most of them can be understood readily as due to circulation of histamine or histaminelike substances formed as the result of exposure of the skin, which have entered the circulation. These effects give scientific support to the public opinion that exposure to sunlight may produce in healthy individuals an increased feeling of well-being, increase of appetite, and facilitate muscular activity.

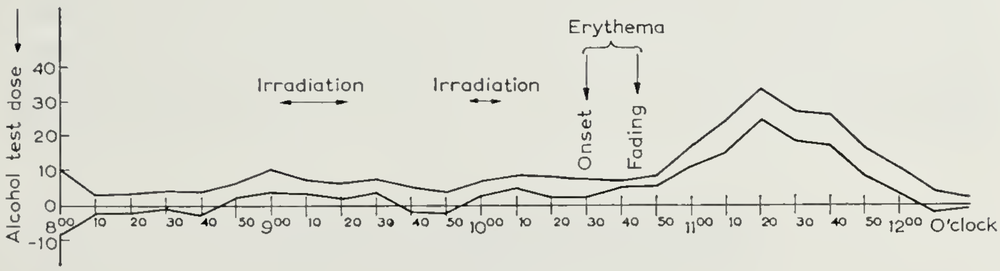


Fig. 57.
Influence of ultraviolet light upon the secretion of gastric juice in the human subject (after Diehl) (according to Ellinger[987]).

(1) *Effects on the gastrointestinal tract.* As the result of exposure to erythema-producing doses of sun- or artificial-ultraviolet light, increased gastric secretion has been observed in normal subjects as well as in patients (Diehl[981], further details and literature by Ellinger[987]) (see Fig. 57). Severe overexposure to ultraviolet light may produce inflammatory changes of the stomach (gastritis).

(2) *Effects on the circulatory system.* They consist in a fall of the *blood pressure,* first observed by the Danish physiologist, Hasselbalch[1005], in 1905. In healthy young adults the fall may amount to 6 to 8 mm Hg (Johnson *et al.*[1058]). The fall in blood pressure is related to the dilatation of the capillaries of the skin due to the liberation or new formation of histamine substances in this organ under the impact of irradiation (Harris[1004]). The effects of ultraviolet radiation on the formed elements of the blood are very contradictory (for refs., see Ellinger[987]). Increases in the *number of erythrocytes* and

the *hemoglobin values,* as well as initial increase in polymorphonuclear white cells, have been described. Apparently the presence or abscence of an effect on cellular elements of the blood is largely determined by the starting values prevailing at the observation period. Equally contradictory are the findings with respect to chemical changes of the blood: increases in *calcium, potassium, sodium, and phosphorus contents* have been noted (for refs., see Ellinger[987]), while in normal human beings the blood sugar content appears to remain unaffected (Lippman and Völker[1031]). Of scientific interest is the observation that serum, obtained from rabbits exposed to sunlight, loses its vasoconstrictor properties, as demonstrated in pharmacological studies by Feldmann and Azuma[995] in 1928, an observation which seemed to point to the presence of histamine-like substances. A direct influence on the blood-histamine level was demonstrated in dogs exposed to an artificial ultra-violet source (carbon arc) by Laurens and Von Kolnitz[1026].

(3) *Effects on metabolism** There exists a host of investigations on this subject. A reduction of the *respiratory quotient* has been observed after acute exposure of man, but the basic metabolic rate remained unchanged. Repeated exposures may, however, cause a reduction of basal metabolism. *Mineral metabolic changes* are reflected in observations on blood chemical

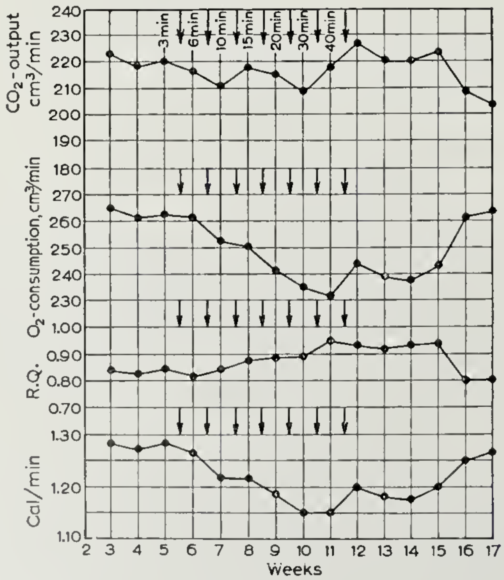


Fig. 58.
Variations in the basal metabolism and total metabolism with prolonged ultraviolet irradiation (after G. Lehmann) (according to Ellinger[987]).

* For details, see Pincussen[1046], Laurens[1025] and Ellinger[987].

changes. *Protein metabolism* appears increased, as manifested by increased urinary nitrogen excretion. Of particular interest are observations indicating a beneficial influence of ultraviolet radiation on work output (Lehmann *et al.*[1028-1030]) (see Fig. 58). These effects, too, are closely associated with erythema production. They have been confirmed by numerous investigators (see Ellinger[987]).

(4) *Effects on ductless glands.* Among these effects those on the *thyroid* appear of special interest (see p. 567). An effect has been deduced indirectly from the observation of a thyroid hyperplasia which occurred in rats[965], rabbits and cattle[1053], and fowl[1063] reared in the dark. In hyperthyroid persons exposure to ultraviolet may cause an exacerbation of their hyperthyroidism (Ellinger[987]).

Ultraviolet irradiation influences the content of the *adrenal cortex* on fat-staining with sudan (Langendorff and Lorenz[1024]). Changes in sudanophile fat of the adrenal cortex are considered to indicate a change in the activity status of this organ. This can readily be explained as the result of histamine in the circulation (Ellinger[987]).

Clinical evidence seems to point to an influence of ultraviolet on *ovarian* function (Kirchoff[1020]).

*3. Biological Effects of Infrared Radiation (Heat Rays)**

by

F. P. ELLINGER

From the physiological point of view, infrared rays of sunlight rank next to ultraviolet radiation.

* Note by S. W. Tromp: Bazett classified the infrared part of the sun spectrum into three parts: *near infrared* (λ = 7,800–15,000Å), *intermediate infrared* (λ = 15,000–30,000Å) and *far infrared* ($\lambda >$ 30,000Å) The part with $\lambda <$ 30,000Å is known as *penetrating infrared*, the longer wavelengths as *non-penetrating infrared*. The skin temperature is elevated highest by the non-penetrating infrared because part of the visible and penetrating rays are reflected by the skin. According to Hardy and Oppel the smallest rate of radiation which the body can perceive as heat is $15 \cdot 10^{-5}$ gcal/cm^3/sec which is equal to one nine-millionth of the normal hourly radiation loss from the body surface. The skin temperature change caused by this radiation is a total elevation of 0.003° C.

Sunlight penetrates the human skin only a short distance. Maximal penetration in the skin occurs at about 7,500Å (according to Bachem and Reed), 99% of the radiation being absorbed after penetrating a few millimeters. Wavelengths shorter than 3200Å do not penetrate more than 0.1 mm.

Depending on the height of the sun, the amount of cloud cover and the composition of and vegetation on the soil (re-emitting heat waves) up to a maximum of 1.8 gcals/cm^2/min can be received as heat load of solar radiation. Blum estimated the total radiation load received by an erect man up to 340 kgcal/m^2/h (which, according to Ladell, is equal to walking at 5 km/h in full military equipment). It should be kept in mind that also on a sunless day due to indirect radiation from the soil or dust in the sky considerable heat radiation can be experienced.

Local effects on the human body

(1) *Effects on the human skin.* Infrared radiation produces an erythema (reddening) of the skin. However, in contrast to ultraviolet erythema, infrared or heat erythema becomes manifest immediately after exposure and disappears within a few minutes after irradiation. Usually, it is not followed by pigmentation, but repeated exposures to infrared may cause a *heat pigmentation**. The effects of infrared on the skin are not different from those produced by heat conduction.

(2) *Effects on the eye.* Most of the infrared radiation is absorbed by the conjunctiva and cornea; therefore these parts are primarily affected. Irradiation produces a painful inflammation of the conjunctiva and cornea, clinically designated as *photoophthalmia.* The changes are similar to those produced by ultraviolet, but occur more rapidly (Cogan[980]).

Formation of cataracts by chronic exposure to infrared is established beyond doubt. Since infrared radiation of 10,000 Å penetrates to the retina, the occurrence of retinal lesions is not surprising (for detailed refs., see Ellinger[987]). They may be produced by careless observation of the sun during an eclipse with the eye not protected by darkened glasses (Tower[1062], Wadenstein[1065]).

General effects on the human body

They are not different from those produced by heat conduction and are, therefore, beyond the scope of this article.

4. *Biological Effects of Visible Light*

by

F. P. ELLINGER and S. W. TROMP

Effect of spectral colours (by F. P. Ellinger)

Radiations with wavelengths between 3800 and 7800 Å emitted by the sun are perceived by the human and animal eye, hence the name "visible light". On this part of the solar spectrum depends our visual concept of our environment, as well as plant life. In general, the proverbial statement "No life without light" holds good, but man and animals can exist in darkness if proper nutritional conditions are provided**.

* The medical designation of this pigmentation is cutis marmorata.

** Detailed discussion of the visual perception of light, as well as its importance to general health and for the growth of plants (photosynthesis of carbohydrates and chlorophyll) is beyond the scope of this article and the reader is referred, for details, to textbooks on human, animal-, and plant-biology.

Very little is known about the effects of spectral colours of visible light on the human and mammalian body (for details, see Ellinger[987]). The human skin seems to possess a rudimentary sensory organ for spectral colours (Ehrenwald[984, 985]). An indirect effect of red light perceived by the eye and mediated via the pituitary gland to the gonad has been demonstrated experimentally in ferrets by Bissonnette[967] and Benoit (see below).

The emotional effect of spectral colours on man was first pointed out by the famous German poet, Johann Wolfgang von Goethe (1749-1832), in his treatise *Farbenlehre*. Its general recognition is reflected in the French term "rouge érotique". A mechanism similar to that established experimentally in ferrets might be adduced for the scientific basis of this popular term. Modern public buildings (hospitals, office rooms, etc.) use the emotional effects of spectral colours to good advantage.

Effect on hypothalamus and pituitary (Benoit-effect) (by S. W. Tromp)

Whereas in the previous section the psychological aspects of visible light were stressed, a few remarks will be made in the present section on the interesting studies carried out by Benoit (Professor of Histophysiology, Paris) and confirmed by Milin[1107–1112] in Yugoslavia. The experiments performed by Benoit, Assenmacher and their collaborators[1067–1082] were briefly reviewed on p. 261. It was stated that light stimulation increases the size of the testicles of ducks, a phenomenon which is prevented by the removal of the anterior lobe of the pituitary. Benoit was able to show that irradiation of other parts of the body of ducks (after removal of the feathers) did not affect the gonades or testicles. Also covering of the eyes of ducks has a preventive effect. On the other hand, removal of the eyeball does not affect the increase in size of testicles. Hence the eye facilitates only the *penetration of light waves into the hypothalamic region,* but is not essential.

Experiments with *monochromatic light* demonstrated the following: (*i*) Direct stimulation of the hypothalamus is possible with all wavelengths from indigo to red. The retina reacts only to orange and red. (*ii*) Yellow radiation has no optical effect, although the eyes of birds (*e.g.* pupil diameter) have a maximum sensitivity to this wavelength. This suggests that the effects of lightwaves, in case of visual and hypothalamic stimulation, are different.

As stated on p. 261, Milin was able to confirm Benoit's observations at the Institute of Histology and Embryology of Sarajevo (Yugoslavia). Thirty days of continuous illumination produced hypertrophic nuclei of the hypothalamus.

Effect on vitamins (by S. W. Tromp)

It is known that the vitamin B_1 (thiamine) content of plants (and therefore of our food) changes with the temperature, light intensity and dayly number of sun hours. Recent studies by H. Ruge (Professor of Botany at the Botanical Institute at Hanover, Germany) have shown that biosynthesis of this vitamin is slightly increased by light waves larger than 630 mμ; it increases considerably with light waves of 435 mμ–505 mμ.

Light waves between 505 and 630 mμ (in particular 535 mμ) have a retarding effect. The same happens with $\lambda = 395$ mμ (for further details see *Z. f. Naturforschung,* (1959) 582–584).

Undoubtedly similar relationships exist for other vitamins and for various important organic compounds in plants used for human consumption, which may explain at least part of the indirect influence of sunlight on the human body and the seasonal variations in the effect of trace elements.

Physiological influence of complete darkness (by S. W. Tromp)

(1) Benoit, Assenmacher and Brard[1078] also studied the influence of complete darkness in relation to seasonal changes in gonad activity of birds. For the same species the period of maximum and minimum activity is fairly constant but varies for different types of birds. Five young ducks were kept for 3 years in a dark room. Each day the size of the left testicle was measured and compared with a duck kept in the open air. The following results were obtained: (*i*) The development of the growth of testicles of the animals kept in the dark was normal. (*ii*) Each year there was a decrease in size from October to March, followed by an increase. This cycle was the same in all 5 animals but different from the control and from the astronomical light cycle. In the controls in the open air the maximum development is reached in May, about one month before the summer solstice. The experiments in dark environments suggest that light is not the only factor responsible for the animal cycle and that it only seems to accelerate the rhythm initiated by gonad-stimulating processes of the hypothalamic-pituitary system.

(2) Milin[1110] studied the effect of 30 days of complete darkness on the hypothalamic structure of the brain of rats. He observed various regressive structural changes, the neuro-glandular cells being smaller than usual with unequal nuclei and small nucleoli, etc.

(3) On p. 261 we referred to the observations of Fuchs[1307] and Hollwich[1097] indicating different pituitary functions in the blind.

5. *Possible Effects of Polarized Light*

by

S. W. TROMP

In the previous sections we discussed the general effect of solar radiation but did not enter into the possible influence of the degree of polarization of the sun's rays. We speak of light as being *polarized* when the wave motion of the electromagnetic energy, traveling in the direction of a light ray, moves in one particular plane only and not in all directions perpendicular to the light ray.

Light reflected from the surface of water, snow or ice is partly polarized perpendicular to the plane containing the incident and reflected light rays; the broken light ray, penetrating the medium, is partly polarized parallel to the plane of incidence. Also light coming from the blue sky is partly polarized, as was discovered in 1809 by Arago. According to Rayleigh, the polarization of sky light is due to the scattering of light caused by air molecules or other particles, small in comparison with the wavelength of light. If the light is scattered perpendicular to the sun's rays it is completely polarized in a plane containing the incident and scattered rays; it is less polarized in other directions.

The polarization of sunlight is maximal in light coming from a region 90° from the sun. In this case almost 2/3 of the sunlight are polarized perpendicular to a plane containing the sun, the observed point and the observer. Near the solar vertical there are three small regions with non-polarized light, *viz.*, 160° from the sun, 20° above it and 20° below it. The degree of polarization of light received by the human body varies continually and depends on the sun's altitude, the wavelengths of the light reaching the earth's surface, the degree of turbidity of the atmosphere, air pollution, cloudiness and so forth.

Little is known about the physiological significance of polarized light to the human body. In the animal world it does play an important part in many organisms. K. von Frisch[1119] (Professor of Zoology at the University of Munich, Germany) demonstrated in a series of ingenious experiments that the fixed compound eye of insects, like *honey-bees,* is able to recognize the direction of polarization of sunlight. This process governs the orientation of bees'dances, for example, which, according to von Frisch, indicate the distance and direction of a favcurable feeding place for the other bees. Miss Schifferer, a pupil of Von Frisch, was able to prove that *ants* orientate themselves by means of the polarization of the light in the sky. G. Kramer demonstrated that *starlings* will fly during the period of bird migration in certain directions related to the polarization of sunlight, not the location of the sun as such. Several Crustaceans (like *Daphnia*) too, use the polarization of sunlight as a means of orientation. Among the Arthropods the *Limulus* (horseshoe crab) possesses a light polarization analyzer in the compound eye (studies by T. H. Waterman[1120-1121]).

These few examples illustrate the sensitivity of various lower animals to polarized sunlight. So far, systematic experiments have not been carried out on the difference in biological effects of ordinary and strongly polarized sunlight on the human skin and eye. Bioclimatology still awaits an answer to this interesting question.

6. *Influence of Photodynamic Substances*

by

F. P. ELLINGER

The presence of substances usually exhibiting the physical phenomenon of fluorescence, has been recognized as the *cause of light sensitization*. Under this term an abnormal reaction of the skin, from the qualitative as well as the quantitative point of view, is understood, *i.e.*, sunlight with wavelengths which ordinarily may not produce an erythema or pigmentation of the skin may do so; and usually ineffective sub-threshold radiation doses may produce these skin effects.

The first observations along these lines were made by a young German pharmacologist, Oskar Raab[1048], who described how the addition of a dilute solution of the fluorescent dye acridine to a colony of Paramecia killed these more readily if exposed to sunlight than if kept in the dark. In later studies it was shown that a similar effect could be obtained with numerous other fluorescent dyes and also if such dyes were injected into mammals (mice). For the phenomenon of sensitization to sunlight by fluorescent substances of various origins (plant materials, metabolites, etc.), Von Tappeiner[1060] coined the term "*photodynamic action*"*. Substances which produce a photodynamic action are called *photosensitizing agents*.** With respect to their role in producing skin diseases, they are classified as either *endogenous* or *exogenous* agents. According to Haxthausen and Hausmann[1007]

* For a list of photodynamic substances and their actions, see the monograph by Blum[970].

** Note by S. W. Tromp: In recent years a new kind of photosensitizing agent has been discovered in the form of certain sulphonamide drugs often applied in modern medical treatments. Due to the influence of light the sulphonamide may be oxidized into a substance (*e.g.* *p*-hydroxy-aminobenzolsulphonic acid amide) which acts as an antigen. In 1957 Burckhardt and Schwarz-Speck described the appearance of a rash and vesicles on the skin of patients 10 or more days after the drug was applied, but shortly after exposure of the skin to sunlight.

endogenous agents are substances which may be formed within the body as the result of a metabolic anomaly, *e.g.*, certain porphyrines, or substances which enter the body as drugs administered for therapeutic purposes, such as the sedative luminal, which belongs to the chemical group of barbiturates. Among the exogenous agents belong certain cosmetics (for details, see Ellinger[987, p. 687]).

Photosensitization should be distinguished from "*photo-allergy*" (Epstein[993, 994]), a relatively rare condition in which the process of photosensitization can be transmitted passively from one subject to another by serum injections (for refs., see Ellinger[987, p. 688]).

Subsect. J. INFLUENCE OF AIR IONS ON CERTAIN PHYSIOLOGICAL FUNCTIONS

by

P. KRUEGER, W. WESLEY HICKS and J. C. BECKETT

1. *Introduction*

The notion that atmospheric electricity may exert an influence on the human economy is far from new; as early as 1780 Abbé Bertholon[1124] published a book in which he presented his observations on the response of normal individuals and of patients suffering from various diseases to changes in the electrical state of the ambient air. Over the years a great deal of speculating was done on this intriguing subject, but little was actually accomplished until 1899 when Elster and Geitel[1125] opened the door to quantitation and understanding by demonstrating the existence of electrically charged atmospheric constituents—the classical air ions.

It now became possible to visualize the effects of atmospheric electricity in terms of naturally-occurring ions and to develop the equipment necessary for their measurement and artificial production in the laboratory. These technical advances of the early 1900's provided the springboard for an enormous amount of research directed toward evaluating the therapeutic properties of air ions and, to a lesser extent, toward determining the physiological and histological responses of experimental animals to air ions.

The literature is replete with clinical reports of the effects of air ions on a great variety of diseased states. The published results vary from well-controlled studies encompassing adequate numbers of patients and careful objective measurements to sketchy observations of subjective changes in a few patients, conducted with little regard to such important factors as ion dosage, adventitious gaseous by-products or essential controls. Despite this unfortunate disparity in quality it is remarkable that the large body of investigators responsible for these tests agree with impressive unanimity that negative ions in general are beneficial and positive ions harmful to the recipient. An answer to the question "Why are these qualitatively different effects achieved with ions of opposite charge?" has been the goal of a number of laboratory programs; although some progress has been made, the ultimate solution remains to be attained.

To begin with, there is something of an intellectual effort involved in accepting the idea that an atmospheric ion can exert any sort of biological effect. After all, it is only a group of 4 to 12 gaseous molecules clustered at random around an electrically-charged atom or molecule of gas; it moves slowly, and, as a consequence, wreaks no physical damage on impact. Furthermore, it occurs in strikingly sparse numbers. In an artificially ionized atmosphere, for example, the ratio of ion groups to non-ionized molecules is of the order of 1 to 20 trillion.

That the body of a metazoan can detect these ionic clusters among the astronomically more prevalent un-ionized molecules and react with them seems something more than improbable at first glance. Nevertheless, one can advance reasons that make this possibility a good deal more acceptable.

2. *The Nature of Ions*

First, it should be understood that ions are unique constituents of the atmosphere; the basis for their unusual properties is to be found in the electrical charge of the key molecule that binds the adjacent 4–12 uncharged molecules to it in what might be described as a raft of molecules. The myriads of ordinary molecules interspersed between neighboring ions are uncharged and in consequence possess distinctly different physical properties. They don't, for example, move in an electrostatic field, nor do they readily react with particulate or gaseous constituents of the atmosphere. Gaseous ions, on the other hand, do these things; it may be inferred then that their unusual physical attributes will condition the type of physiological response they evoke.

Granted the singular character of these electrically charged molecular groups, one need not be too surprised at the body's ability to ferret them out. This imposing feat is performed readily and accurately by laboratory equipment commonly used to determine the numbers of ions present in air (ion collector and micro-microammeter). The fact that a number of mammalian tissues possess exquisitely sensitive receptors that respond to a variety of minute mechanical and chemical stimuli, is sufficient reason to make one entertain the possibility that the body may be capable of duplicating this operation.

3. Effect of Air Ions on Cells and on Respiration

Effect on cells

It will be useful, perhaps, to summarize the relevant data from a representative group of published studies in which experimental conditions were controlled and reproducible changes were induced as a result of air ion action on cells. An important factor in the succesful performance of most of these recent experiments has been the development of an ion source (Fig. 59) capable of producing high yields of unipolar ions free from gaseous contaminants[1138, 1123]. Radiation from ^{210}Po or ^{3}H, respectively, creates ion pairs; a rectifying circuit removes the unwanted ionic type while directing the selected ion to a target, *e.g.*, a tissue or cell suspension. We purposely exclude from consideration in this section the large number of clinical papers concerned with air ion effects on various diseases.

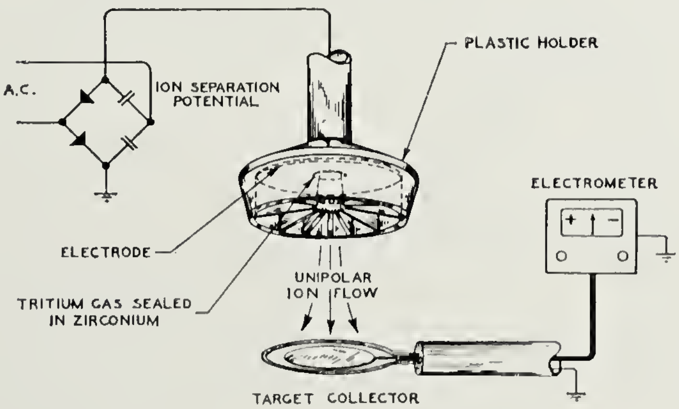


Fig. 59.
Radioiosotope source of air ions showing arrangement for separation and for measurement of ion rate of flow (after Krueger, Hicks and Beckett).

Turning first to the direct action of air ions on cells, we find that several investigators have performed experiments in which indirect effects through the circulation or central nervous system either are completely ruled out or at least are not necessarily involved.

The former situation obtains in the case of small air ions acting on staphylococci[1134]. Although preliminary experiments had established that staphylococci dispersed in liquid media or on various types of enriched agar and then exposed to high densities of air ions failed to display detectable changes, positive results were obtained when special experimental conditions were imposed. By adapting the equipment and methods of microchemistry to

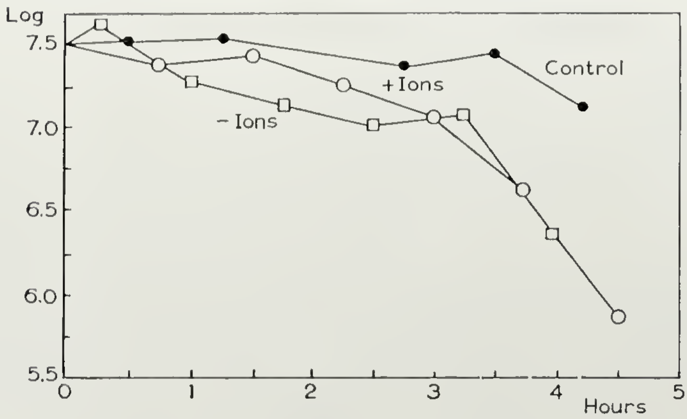


Fig. 60.
Acceleration of the death rate of staphylococci suspended in 50-λ evaporating droplets in the presence of negative and positive air ions. Data: 1.6·10⁹ ions/cm²/sec at 4 cm; relative humidity 48%; bacteria remaining after 4.5 hours (after Krueger, Hicks and Beckett).

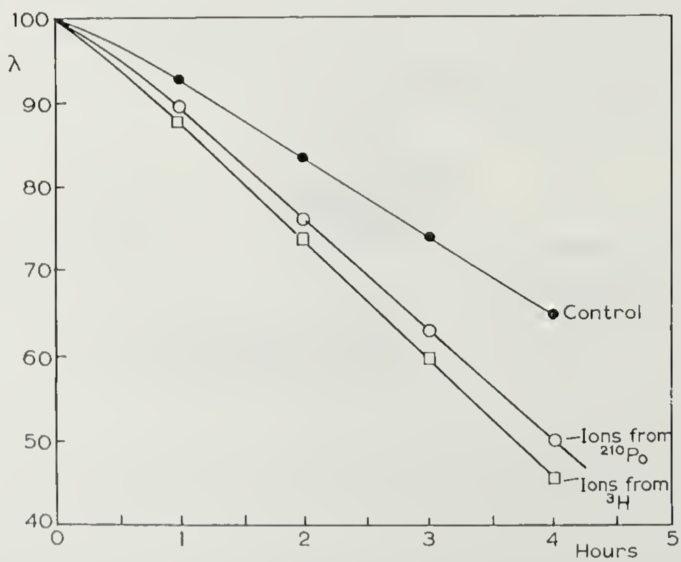


Fig. 61.
Acceleration of evaporation rate in the presence of negative ions derived from two radioisotopes. Relative humidity 78%; fluid remaining after 4 hours (after Krueger, Hicks and Beckett).

permit accurate handling of small drops of cell suspensions, by using droplets sufficiently small to provide a high ratio of surface to volume (7–100 λ), and by employing distilled water as the suspending medium, measurable changes in the survival curves could be demonstrated.

If a 50-λ droplet of staphylococcal suspension was allowed to evaporate n clean air during exposure to densities of ca. $1 \cdot 10^9$ + or − air ions/cm²/sec, the death rate was appreciably accelerated (Fig. 60). This rather moderate lethal effect did not involve any change in pH or Eh, but a contributing factor may have been an observed increase in the rate of water evaporation (Fig. 61).

When the volume of the droplet was kept constant, no shift in the slope of the survival curve occurred unless the suspension was stirred (Fig. 62); then there was an appreciable rise in the rate of death, the decrease in viable cells per unit of time being the same in negatively and positively ionized atmospheres. Since the data obtained in these experiments were derived from colony counts it was essential to rule out spurious drops in the number of viable survivors due to agglomeration of cells. No clumps were found on microscopic examination; further, when the Von Smoluchowski equation[1139] was used to predict the minimal time required for agglutination in the light cell suspensions used, the observed values of t for a lethal effect were considerably lower than the calculated values.

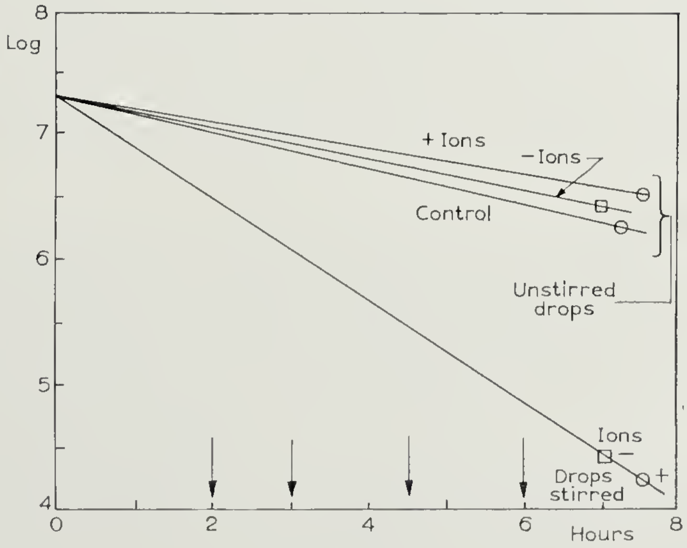


Fig. 62.
Acceleration of the death rate of staphylococci from stirring 50-λ droplets in the presence of unipolar air ions. Volume of droplet kept constant by additions of distilled water. Relative humidity 40%; bacteria remaining after 8 hours (after Krueger, Hicks and Beckett).

Similar experiments on the effects of small air ions on staphylococcal suspensions were conducted (inadvertently) in smog-polluted atmospheres. The results were altogether different because the pollutants tended to remove ions from the air; details are omitted here since they do not contribute to the immediate subject of this chapter other than to emphasize the dependence of air ion-induced physiological effects on the cleanliness of the ambient atmosphere.

Evidence of a lethal effect due to air ions was obtained by Fuerst and Ball[1127] in a carefully conducted series of experiments with several strains of *Neurospora crassa*. They found that both negative and positive air ions in densities of approximately $1 \cdot 10^5$/ml produced moderate but significant increases in the death rate of exposed conidia.

Worden[1141] has observed direct effects of air ions on tissues growing *in vitro*. Halves of chick blastodiscs were grown in Carrel flasks containing a suitable medium and so arranged that the temperature, humidity and ion content of the ambient air could be controlled. In each instance one-half of the blastodisc served as a non-ionized control while the other half was exposed to air enriched with unipolar ions. The matched pairs were incubated in the same incubator and at the same time.

Dimensions of the explants were determined at the start of the experiment and after 72 hours of incubation. Statistically significant growth acceleration occurred in the explants exposed to negative air ions and growth inhibition in those exposed to positive air ions. More recently Worden has found that Earle's Strain "L" cells grown *in vitro* react similarly to unipolar air ions[1142].

Effect on respiration

Winsor and Beckett[1140] have reported interesting experiments in humans which furnish further evidence of direct action of air ions on tissues. Exposure to atmospheres containing high densities of positive air ions produced "dryness, burning and itching of the nose, nasal obstruction, headache, dry, scratchy throat, difficulty in swallowing, dry lips, dizziness, difficulty in breathing, and itching of the eyes". Negative ions did not produce these full-blown symptoms, but occasionally caused mild discomfort.

The influence of air ion inhalation on the maximal breathing capacity was studied by sealing the mouth with adhesive tape and having the subject breathe forcibly through a face mask. The five individuals tested were able to breathe on the average 35 l/min under normal conditions. After a preliminary exposure to positive air ions the maximal breathing capacity dropped to 25 l/min; similar pre-treatment with negative air ions produced no detectable deviation from the controls. The reduction apparently was due to swelling of the nasal mucosa induced by positive air ions. This corroborates and extends the earlier observations of Yaglou *et al.* on irritation of the upper respiratory tract following inhalation of positive air ions[1143].

4. Experiments on Mammalian Trachea

During the past two years studies have been in progress at the University of California in Berkeley on the response of the mammalian trachea to unipolar small air ions (see p. 301). The trachea was selected because of its easy accessibility and because it is lined with a mucosa representative of that covering the respiratory tree from the epiglottis to the respiratory bronchioles. The unique combination of cells with cilia on their free border and cells capable of forming mucus provides the anatomical structure that permits the specialized and very important clearing mechanism of the respiratory tract to operate. Any inhaled particulate matter such as pollens, dust, or bacteria ultimately is trapped in the mucous film coating the epithelium and becomes a passive passenger in its cephalad flow. This flow is largely dependent on the wave-like action of the cilia beating at rates approximately 800–1000/min. (see p. 452).

To conduct experiments on tracheal function, a glass and plastic chamber was constructed (Figs. 63 and 64) which permitted microscopic observation of an enclosed tracheal strip in an atmosphere maintained at *ca.* 23° C and a relative humidity of $> 80\%$. A tritium ion generator protruding through the roof of the chamber was equipped with a reversible rectifying circuit allowing selection of ions of either charge. By watching the ciliary movement while the surface of the tracheal strip was illuminated by a strobotachometer it was possible to determine the rate of beat with an accuracy of $\pm$ 50 beats/min. The rate of mucus flow was measured by timing the progress of air bubbles trapped in the mucous film along the grating of an eye-piece micrometer. The general effects[1129] observed in excised tracheal strips from rabbits, guinea pigs, mice, and rats are presented in Figs. 65 and 66. In addition it was noted that positive ions:

(1) Caused the membranous posterior wall of the trachea to contract; in this condition the peristaltic wave normally produced by stretching the tissue laterally could no longer be elicited. Here again treatment with negative ions reversed the positive ion effect, the posterior wall relaxed and the peristaltic reflex was re-established.

(2) Dried the mucosal surface. Negative ions either had no effect on the surface or brought about the appearance of a watery fluid.

(3) Rendered the cilia remarkably vulnerable to mechanical traumata. A single, very gentle stroke with a moist cottontipped applicator that had no lasting effect on the control, but completely abolished ciliary activity over the area treated with positive ions. This state of enhanced vulnerability disappeared gradually if the strips were permitted to stand in an un-ionized

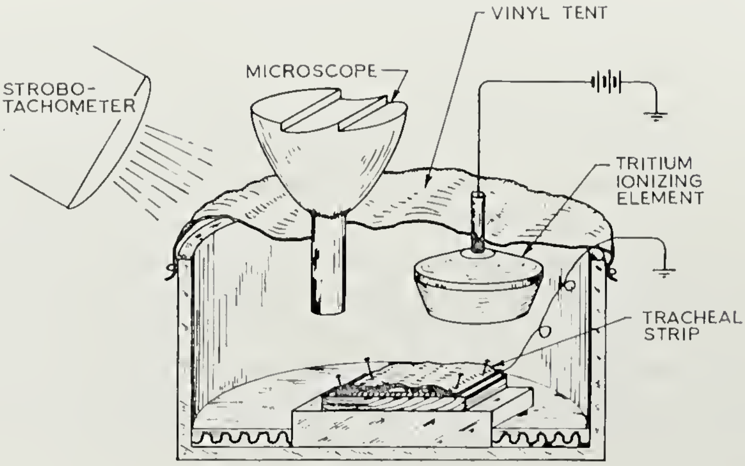


Fig. 63.
Experimental arrangement for exposure of tracheal strip to unipolar air ions to observe mucus flow and ciliary activity (after Krueger, Hicks and Beckett).

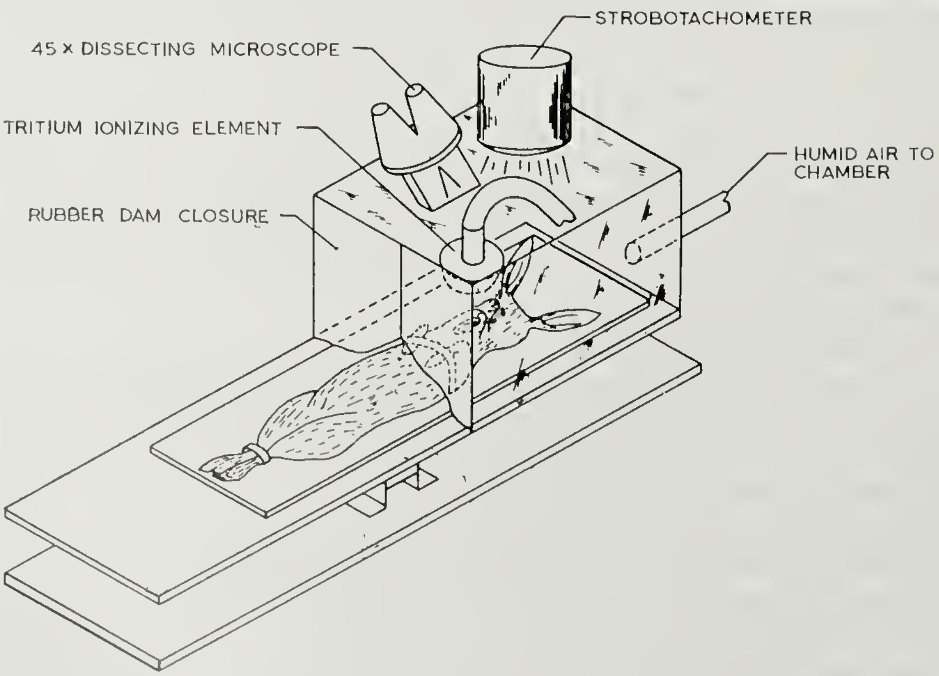


Fig. 64.
Experimental arrangement for exposure of trachea of live animal to unipolar air ions (after Krueger, Hicks and Beckett).

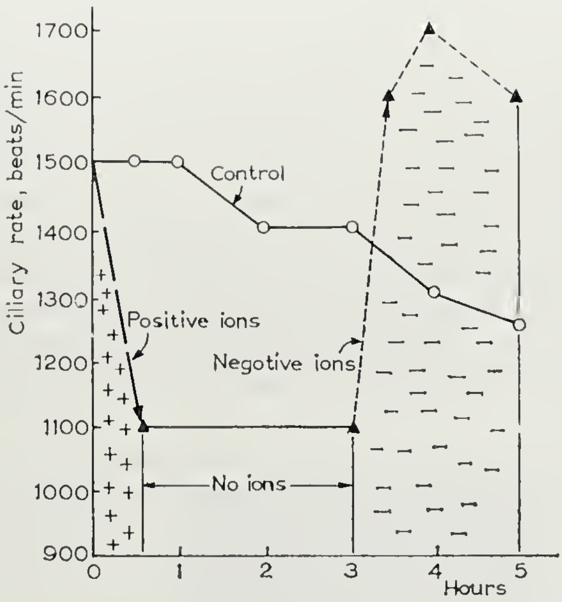


Fig. 65.
Effect of unipolar air ions on the ciliary beat rate of tracheal strips (after Krueger, Hicks and Beckett).

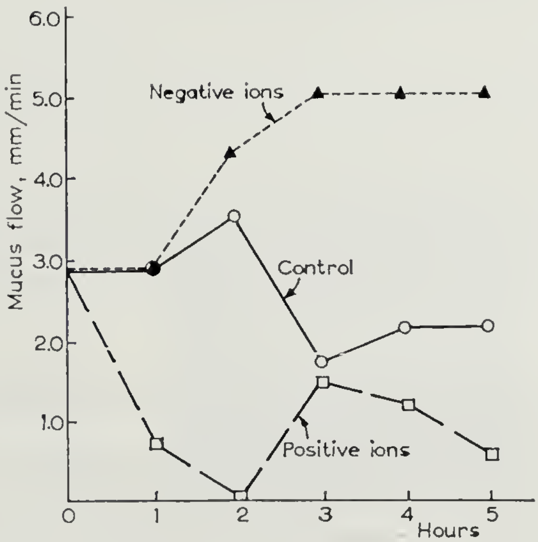


Fig. 66.
Effect of unipolar air ions on the mucus flow of tracheal strips (after Krueger, Hicks and Beckett).

atmosphere for one hour or quite promptly if the tissue was treated with negative ions.

Subsequently, these experiments were repeated on living rabbits, rats, mice, guinea pigs and monkeys, administering the ions directly to the mucosa through a tracheotomy aperture[1130]. Positive ions produced the same sort of changes noted in the isolated strip, and, in addition, there was apparent clear-cut evidence of increased irritability of the mucosa. The slightest pressure with a probe produced either a web-like network of dilated capillaries or a disc-shaped ecchymosis in the mucosa of the trachea exposed to positive ions but evoked no such response in non treated controls or in animals treated with negative ions. This reponse was especially marked in animals such as the rabbit, whose tracheal walls are characterized by an abundant vascular supply.

The inhalation of moderate densities of air ions by intact (un-operated) ambulatory mice brought about similar but not identical functional changes. With positive ions these consisted of decreased ciliary activity, paleness and contraction of the posterior tracheal wall, and enhanced vulnerability to trauma; there was no clear cut effect on mucous flow. Negative ions increased the rate of ciliary beat but did not alter the flow of mucus.

It was found that an exposure period of 60 minutes sufficed to initiate these changes and that, once established, they tended to persist. For example, groups of mice were kept in non-ionized and unipolar-ionized atmospheres for three days; at intervals thereafter individuals were removed, anesthetized with rectally administered penthobarbital, tracheotomized, and the condition of their tracheas studied by the techniques already described. Typical positive and negative air ion effects were uniformly encountered even four weeks after exposure to ionized atmospheres—while animals maintained in untreated air showed no changes (see also p. 611). This is a rather surprising result for which we can offer no ready explanation, but it occurred so regularly in all the animals studied that we are convinced of its validity.

5. *Gaseous Ions Responsible for Tracheal Response*

In experiments such as these all the gaseous components of the atmosphere are subject to ionization and it would be difficult to infer *a priori* which particular gases in ionic form mediated the positive and negative effects (see p. 301). Consequently, a series of tests was conducted on the ciliary activity of tracheal strips, replacing the air in the ionization chamber with various gases[1131]. Negative ion effects were observed only when oxygen was present; none occurred when the chamber was filled with nitrogen or carbon dioxide (Fig. 67). When conditions for positive ion formation were imposed, typical results were obtained with carbon dioxide and none with nitrogen or oxygen (Fig. 68). It was concluded, therefore, that negatively charged oxygen and positively charged carbon dioxide are the mediators of physiological effects occurring in the trachea as a result of atmospheric ionization.

Additional work was done on this subject more recently using living rabbits[1136]. An area for observing gaseous ion effects was prepared by tracheal fenestration just caudal to the larynx. This zone was isolated from the lower trachea, bronchi, and lungs by intubating the trachea very close to the manubrium sterni, thus providing a separate airway through which respiration cold be carried on while gases such as nitrogen and carbon

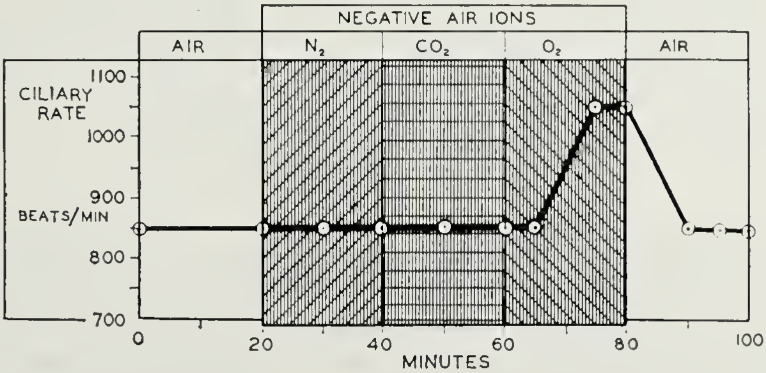


Fig. 67.
Increase in ciliary activity in the presence of negative ions observed only in combination with oxygen gas (after Krueger, Hicks and Beckett).

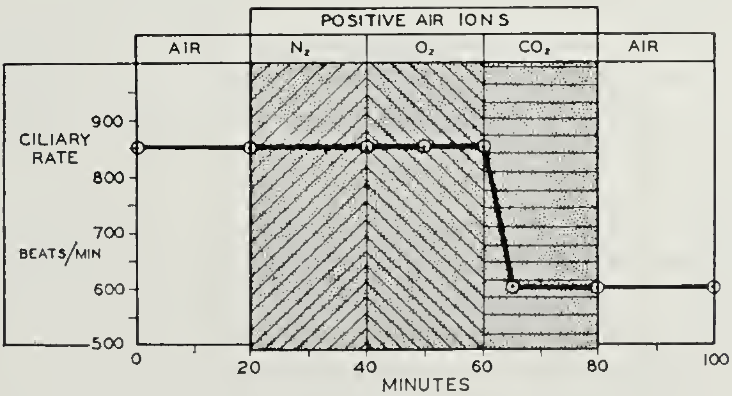


Fig. 68.
Decrease in ciliary activity in the presence of positive ions observed only in combination with carbon dioxide gas (after Krueger, Hicks and Beckett).

dioxide filled the upper trachea[1139]. Using an exposure period of 20 minutes and maintaining a relative humidity of $> 90\%$ throughout the experiments it was found that non-ionized nitrogen, oxygen and carbon dioxide had no effect on ciliary activity nor did they elicit the E.V.T. (enhanced vulnerability to trauma) response. Under conditions permitting the formation of negative ions, negatively charged oxygen raised the rate of ciliary beat but did not increase vulnerability to trauma; nitrogen and carbon dioxide were without effect. When the rectifying circuit was reversed to remove negative ions and to send only positive ions through the tracheal window, oxygen and mitrogen produced no changes while positively charged carbon dioxide markedly decreased ciliary activity and evoked a state of E.V.T.

It would appear, then, that direct effects of gaseous ions on individual cells and on tissues can be detected. In the case of bacteria and molds exposed to ions in clean air the only result demonstrated to date is an increase in the rate of death and this occurs only when the ion content of the air is high. Unipolar ions of either charge produce the same effect. No explanation for the phenomenon has been advanced as yet.

6. A Mechanism for Ion Effects on Tissue

The response of cells organized into tissues is quite different. Positive ions, in general, inhibit growth or activity such as ciliary flicker; they induce the contracture of smooth muscle and enhance vulnerability to trauma. Negative ions accelerate growth and ciliary activity and reverse positive ion effects. How this is brought about is not entirely clear although recent work casts some light on the mechanism of action of negative ions.

The possibility that negative ions may act on one or more of the intracellular respiratory enzymes was suggested by two observations:

(1) Very dilute solutions of sodium azide inhibit ciliary activity;

(2) The hemoglobin of animals sacrificed with carbon dioxide recovers its bright red color more rapidly in a negatively ionized atmosphere than in ordinary air.

Accordingly, a study was made of negative air ion effects on the catalytic activity of a modified Keilin-Hartree pig heart homogenate[1132]. The rate of conversion of succinate to fumarate by the homogenate was followed spectrophotometrically and it was found that the rate was accelerated by negative air ions while positive ions produced no effect (Fig. 69).

To further localize the action of negative ions, experiments were performed on the rate of oxidation of cytochrome-*c* alone and on cytochrome-*c* + heart homogenate. Positive and negative air ions were without effect on the

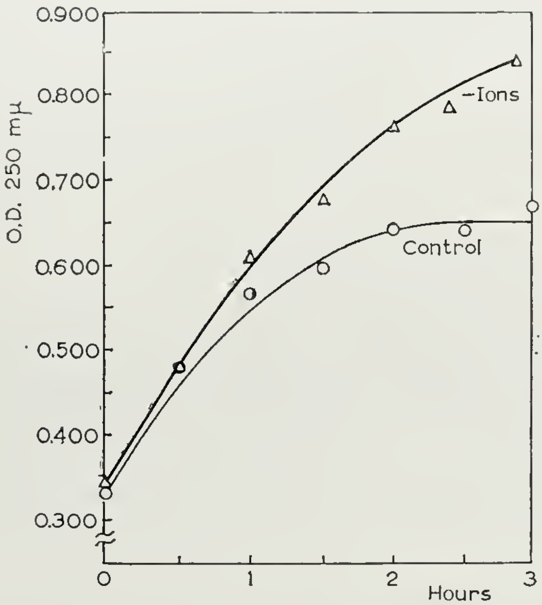


Fig. 69.
The rate of conversion of succinate to fumarate by a Keilin-Hartree pig heart homogenate in normal and negatively ionized atmospheres (after Krueger, Hicks and Beckett).

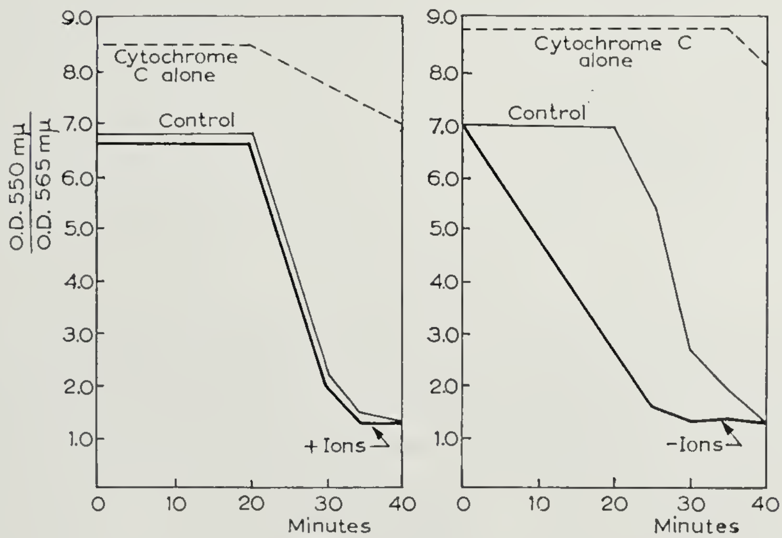


Fig. 70.
The re-oxidation by cytochrome oxidase in normal and ionized atmospheres of cytochrome-*c* reduced by sodium hydrosuplhite (after Krueger, Hicks and Beckett).

reoxidation of cytochrome-*c* alone but negative ions had a distinctly accelerating effect when the heart homogenate was added to the solution; positive ions again had no effect (Fig. 70).

Evidently, negative air ions act directly on cytochrome oxidase or what is more probable, they form a radical upon contact with water which then acts directly on the cytochrome oxidase. These observations provide a reasonable explanation for the accelerating effect of negatively charged oxygen on the physiological processes enumerated above, but they do not explain the markedly inhibiting effects of positive air ions.

However, we have in progress a series of experiments which suggest a mechanism for positive ion effects as well. All the tracheal changes attributed to (+) air ions can be duplicated by the intravenous injection of 5-hydroxytryptamine (5-HT). Like (+) ion effects, the 5-HT effects can be reversed by treatment with (—) air ions. On the basis of these facts, it seems reasonable to postulate that (+) air ions are "serotonin releasers," and that a local accumulation of 5-HT in the trachea is the immediate cause of (+) ion effects.

It can further be postulated that (—) air ions reverse (+) ion effects by speeding up the rate at which free 5-HT is oxidized. Like other oxidase systems, monamine oxidase is thought to consist of a dehydrogenase linked to a respiratory chain which may include cytochromes or flavins. Our experiments demonstrating that (—) ions have a direct action on cytochrome oxidase and accelerate the cytochrome-linked conversion of succinate to fumarate would suggest that this same action may produce a cytochrome-linked oxidation of 5-HT.

Experiments with reserpine and iproniazid provide indirect confirmation of this hypothesis.

Reserpine is believed to cause 5-HT to be momentarily released and then rapidly destroyed by monamine oxidase, so that the tissues are quickly depleted of 5-HT. If our hypothesis is correct, reserpine would produce a condition in the trachea resembling that induced by (—) air ions. Moreover, one would expect (+) air ions to be unable to produce their characteristic effects on a reserpine-treated animal, since the 5-HT necessary for (+) ion action is lacking. Both these expectations have been realized experimentally.

In contrast, iproniazid blocks the enzyme responsible for metabolizing 5-HT, so that an accumulation of free 5-HT develops. One would expect an iproniazid-treated animal to display tracheal effects resembling those produced by (+) air ions and to resist the normal action of (—) ions in reversing these effects. Again both these expectations have been experimentally confirmed.

The hypothesis appears to be borne out by experiments just completed in which negative ions decreased the concentrations of 5-HT in extirpated strips of rabbit trachea and in the respiratory tracts of living mice. An initial exposure of guinea pigs to (—) air ions caused a transient rise in urinary excretion of 5-hydroxyindoleacetic acid, the specific metabolite of 5-HT.

7. *Further Experiments with Primates*

Granted that gaseous ions are capable of altering the physiological activity of the tracheal mucosa and the sub-mucosal smooth muscle, and that negatively charged oxygen and positively charged carbon dioxide play opposing roles in mediating these effects, there remain two major questions, *viz.*,

(1) Do these changes take place only in small experimental animals or are they found as well in the primates;

(2) Are these purely laboratory phenomena, dependent on very high ionic densities, or are the physiological thresholds low enough to permit their occurrence in nature?

To answer the first of these questions, tracheal fenestration was performed on each of three *Cynomolgus* monkeys and the mucosa was exposed to air containing high densities of unipolar air ions[1135]. Observation of the rates of ciliary beat and of mucus flow demonstrated that positive and negative ions exerted their typical action (Fig. 71).

On two occasions we were able to test the response of tracheal strips obtained from humans at autopsy[1135]. Here again ciliary activity was affected in characteristic fashion but the mucus film was so sparse that the rate of mucus flow could not be measured.

8. *Dosage*

The second question pertaining to threshold values proved more difficult to answer because of certain technical difficulties encountered in measuring ion densities at lower levels and because there exists a degree of individual variation in susceptibility to air ion action. Nevertheless by using the rate of ciliary flicker in excised tracheal strips from guinea pigs and rabbits and by carefully controlling the conditions of the experiments, it was possible to establish a range of values below which air ion effects seldom occurred and above which they almost always occurred[1133].

When an exposure period of 30 minutes was used the threshold range for

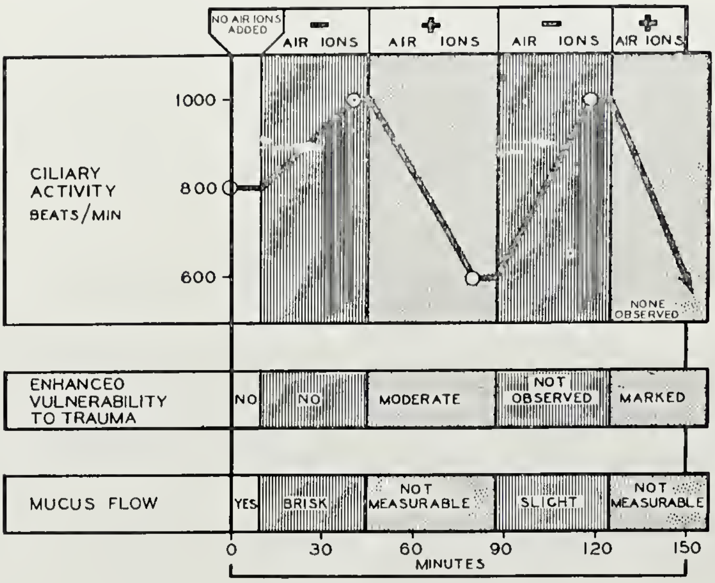


Fig. 71.
Effects of air ions administered through a tracheotomy aperture on clearing mechanism of *Cynomolgus* monkey (after Krueger, Hicks and Beckett).

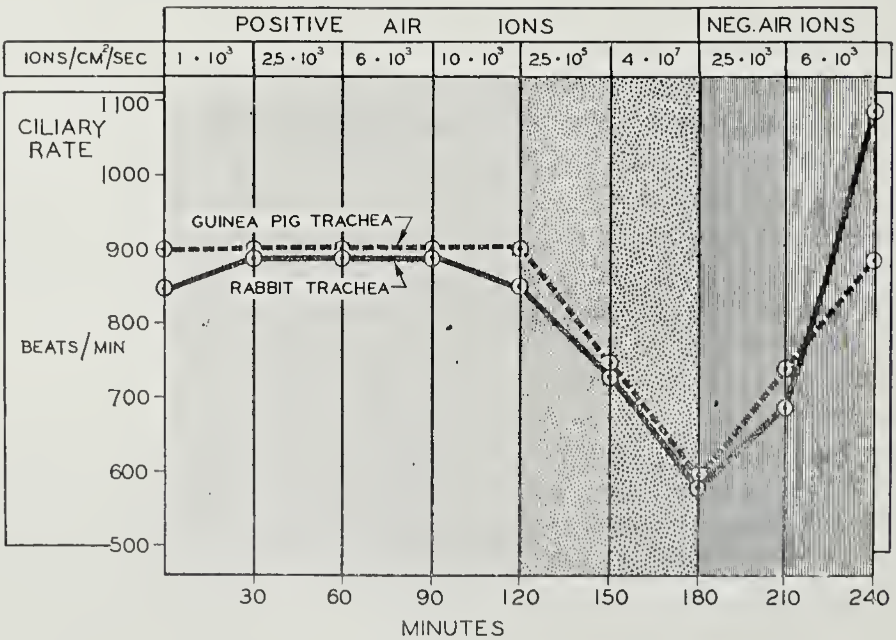


Fig. 72.
Threshold values of air ions affecting ciliary rates of extirpated animal thracheas. Negative ion threshold: $2.5 \cdot 10^3$ ions/cm²/sec, positive ion threshold: $1 \cdot 10^5$ ions/cm²/sec (normal rate of ion flow in clean air at sea level is about $2.5 \cdot 10^3$ ions/cm²/sec) (after Krueger, Hicks and Beckett).

producing a definite effect on the ciliary rate of most animals occurred between $1 \cdot 10^3$ and $1 \cdot 10^5$ ions/cm²/sec. A few sensitive individuals were affected by an air ion rate of flow below $1 \cdot 10^3$ while a few resistant individuals required a rate of flow above $1 \cdot 10^5$ ions/cm²/sec.

In any given animal the negative ion effects occurred at ion densities below which positive ions had ceased to have any effect. Tracheal tissue displaying clear-cut negative ion effects at $2.5 \cdot 10^3$ did not show positive ion effects until the density reached $1 \cdot 10^4$ or occasionally $2.5 \cdot 10^5$ ions/cm²/sec (Fig. 72).

Whatever mechanism is concerned in the change of ciliary rate induced by gaseous ions, the essential condition is direct contact of ions with surface cells. Any action involving the central nervous system can be excluded, for the phenomenon occurs in the isolated tracheal strips as well as in the living animal; for the same reason the transport of ions by the blood stream is ruled out. This places the locus of action in the epithelium and very probably in the most superficial cells since gaseous ions have low velocities and accordingly very little power to penetrate (see p. 71).

9. Discussion

The evidence then suggests that the change in rate of ciliary beat follows from air ion action on some component of the ciliated epithelial cell such as the kinetosome. Other known effects would appear to depend on reaction at different sites, *e.g.*, changes in the nature and volume of mucus present on the epithelial surface, the induction of the condition we have described as enhanced vulnerability to trauma, and contraction of the smooth muscle located in the posterior wall of the trachea. The last two responses involve sub-epithelial elements, *i.e.*, the capillary walls and smooth muscle cells. We have no evidence at present on which to decide whether the ions actually reach the smooth muscle cells and capillary walls or initiate their effect indirectly by triggering surface reactions from which the stimuli are transmitted.

Turning now from the subject of direct effects of air ions on cells, we shall consider some of the evidence that indicates that indirect effects occur. As early as 1931 Happel[1128] reported that positive air ions accelerate and negative air ions decelerate the rate of respiration in human subjects and in anesthetized rabbits. More recently similar results were obtained in our laboratory using rats, treated with chlorpromazine, as the experimental animal[1130]. Both sets of results are compatible with the observations of Yaglou[1143] and Winsor and Beckett[1140] on the tendency of positive ions to produce nasal obstruction in humans. Winsor and Beckett showed that this congestion of the nasal membranes was sufficiently extensive to reduce the maximal breathing capacity by nearly 30%. It seems reasonable to assume that the stimulatory effect of positive ions on the respiratory rate is a compensatory mechanism triggered by a reduction in the effective diameter of the airways. The likelihood of this being the case is increased by our own experimental results demonstrating contracture of the tracheal wall induced by positive ions[1129, 1130]. If the deeper passages of the respiratory tree are similarly affected, the obstruction to air flow would be of considerable magnitude.

An entirely distinct sort of response was reported by Nielsen and Harper[1137] who demonstrated that the succinoxidase content of the adrenal glands of rats maintained in positively ionized air, was significantly reduced; negatively ionized air produced a slight but insignificant rise.

Very recently, Erban at the Institute of Hygiene, Prague, has published an interesting account of tests conducted to detect biochemical changes resulting from the inhalation of air ions[1126]. His subjects were normal males aged 25–45 years and they were exposed to unipolar ions generated by a radioisotope for periods of one hour, three times a week. Ion densities averaged $4 \cdot 10^6$/ml. After 8 weeks of treatment with ions of one sign, each individual underwent a like period of exposure to ions of the opposite charge. Positive ions induced a rise in blood pressure, a decrease in blood albumin, an increase in the globulin fraction of blood, a drop in cholesterol levels and a rise in 17-ketosteroids. The only significant effect of negative ions was to raise the blood albumin and to lower the globulin. Erban concludes that the changes brought about by positive ions are quite similar to those observed during the administration of ACTH.

Rather than close this brief section with a formal "summary and conclusion" we prefer to offer a "situation estimate", for it is clear that we are dealing here with a young and growing subject in which finality is not yet an established characteristic. We feel that there exists today ample evidence that gaseous ions act on individual cells and on cells organized into tissues. The nature of this action is gradually becoming perceptible and as the basic intracellular reactions are understood, it appears to us that practical applications to engineering and medicine will develop on a more rational footing than has obtained in the past. The advances taking place in the broad area of biology have been made possible by rapid strides in the technology of ion generation and ion quantitation. One can now impose conditions for exposure of an animal or human with assurance that a given density of unipolar air ions free from gaseous contaminants is present in the atmosphere.

From this viewpoint it seems reasonable to predict that air ion control of living and working spaces will become routine practice, finding acceptance as an important element in promoting health and comfort[1122]. It may well prove to be a vital factor in establishing optimal environmental conditions for occupants of submersibles and sealed space cabins.

Subsect. K. BIOLOGICAL RHYTHMS

The scientific study of biological rhythms, briefly called *biorhythmics,* is a comparatively new branch of science, which received a major impulse after the creation of the International Society for the Investigation of Biological Rhythm about 20 years ago, the first international conference being held in 1937 in Ronneby, Sweden.

As all living substance, either the body as a whole or its components, is constantly moving, and as external or internal resistances usually prevent unlimited movements, most biological movements, after reaching a certain limit, have to be reversed. When this process repeats itself with more or less constant time intervals, the phenomenon is described as *biological rhythm,* either endogenous or exogenous.

The influence of biological rhythm on the functioning of the autonomic nervous system was briefly mentioned on p. 200. Although a comprehensive discussion of this subject is outside the scope of the present book, a few more general principles will be reviewed in this section in view of the important place biorhythmics holds in biometeorology and bioclimatology.

In the list of references the reader can find a number of interesting publications on this fascinating subject[1144–1201]. Bünning in a recent book, *Die physiologische Uhr*[1161a], has given a most up-to-date review of our present knowledge of this new branch of science.

Endogenous biological rhythms can be observed only if organisms are cut off completely from all external stimuli. The frequency and amplitude of the various endogenous biological rhythms observed differ greatly. Considerable changes in these rhythms may occur as a result of the interaction of external physical rhythms, such as rhythmic variations in light, temperature and humidity of the air, rhythmic fluctuations of the barometric pressure, fluctuations in the electric field of the atmosphere, etc.

In view of the great variety in periodicities, both in the inorganic and organic world, many scientists in various basic sciences are deeply interested in the mechanism and fundamental causes of biological rhythms, for biorhythmics touches many branches of science: biology, physiology, chemistry, geophysics, mathematics, etc. It is therefore a border-science in the true sense.

Despite a vast amount of research carried out during the last 20 years and the introduction of modern methods of statistical analysis, with a few exceptions neither the exact location nor the anatomical structure and physiological functioning of the biological rhythm centres in the living organisms are known. In the following pages a few examples of biological rhythms will be given.

It has been shown by Gerritzen[1170] (the Netherlands), Menzel[1187] (Germany) and others that human diuresis has a 24-hour rhythm with maximum excretion at about 2 p.m. and a minimum at about 2 a.m. This rhythm applies both to the excretion of water and to chloride and urea excretion by the human body. When the experiment is carried out in various parts of the world, this rhythm is found to be determined by local sun-time. Artificial changes in the daily light and dark rhythm of the environment can cause a reversal of the original rhythm.

Rapid (long-distance) air travel is responsible for serious disturbance in this natural rhythm and may even lead to disease. After the Vienna Philharmonic Orchestra travelled to Tokyo by air, it took the members four days to become fully acclimatized. European athletes at the Melbourne Olympic Games had similar experiences. Even more serious consequences can be expected in interspatial travel as planned by *Astronautics*.

Möllerström (Sweden) and Dennemark (Germany) were able to demonstrate, independently, that the hour of the day at which various drugs are administered greatly affects the results of the therapy, depending on the time-phase of the endogenous rhythm.

Several psychiatrists aussume that external stimulation during inhibitory phases of the human nervous system may be responsible for many of the contemporary psychosomatic disorders. Disturbances of the day-night rhythms of the autonomic nervous system (see p. 201) may be responsible, according to various scientists, for peculiar experiences during sleep.

Kleitman[1184], Engelmann, Gifford and other psychologists in the U.S.A. showed that the adaptation of the infant's autonomic endogenous rhythm to the 24-hour activity pattern of the mother creates a sleep-wakefulness rhythm in children long before the third month of life. Gifford (Boston) stated during the Congress of Biological Rhythm in 1957 that "although the highest functions of time-perception are established in later childhood, it is possible that the quality of these early experiences (rhythm adaptations) with time and external reality influences the adult's attitude toward time, his capacity to estimate duration and orientation, his tolerance for frustration and delay, his need for punctuality or freedom from restriction and his ability to adapt or depart from fixed schedules of activity".

Important rhythms have also been reported respecting both the plant and animal worlds, the occurrence of endogenous rhythms in plants having been known for a very long time.

Sir Nigel Ball (London) has recently demonstrated a 24-hour rhythm in the growth of coleoptiles of seedlings in the oat *(Avena sativa)* due to light-dark cycles in the environment. This rhythm can be retarded by lack of oxygen. He also demonstrated that the time-keeping mechanism is not confined to the tip of the coleoptiles.

Cloudsley-Thompson[1162, 1165] (London) has pointed out that in most animals there is a rhythmic alternation of activity, during which feeding, mating and dispersal takes place, with periods of physiological recuperation, the activity usually being linked with the rhythm of daylight and darkness. Rhythms of diurnal and nocturnal activity are common and, in the case of terrestrial arthropods, often related to fluctuating light intensity or variations in temperature and humidity and affected by the waterbalance of the animals.

In the case of insects, a close parallel has been observed between the rhythm of biting activity of certain East African mosquitoes and the bimodal flight activity of the Trichoptera.

Stephens (Minneapolis) has shown the influence of temperature on the 24-hour rhythm of the movement of the melanophore pigment in the fiddler crab, *Uca pugnax,* a light-controlled rhythm previously established by Kalmus (London). The phases of induced rhythms could be shifted by sudden changes in temperature, provided these exceeded certain threshold values.

General problems such as the daily or seasonal time concept, very marked both in plants and in animals, and the observation that many people are able to wake up at pre-fixed hours, are also probably related to certain endogenous and exogenous biological rhythms.

The above examples, a spectrum of the various implications of the theory of biological rhythm, clearly illustrate the importance of this new border science to biometeorology and bioclimatology. The problems involved are extremely complicated and, unless scientists of various disciplines join hands, it will be difficult to penetrate into the deeper causes of the rhythmic activity of the living organism.

Section 2. Physiological Tests to Demonstrate the Existence of Meteorotropism

During the last 50 years many, relatively simple, tests have been devised to demonstrate the influence of weather and climate on physiological processes in healthy man. Although some of these experiments have been discussed in previous sections or will be reviewed in subsequent chapters, a brief compilation will be given in the present section.

In the first column of Table 30 various physiological factors are given which have been studied in the past in relation to weather, climate or season. Some of the results of these studies are summarized in the second column. The third column gives the names of the principal authors responsible for the publications in which the various experiments are described.

This summary clearly indicates that the influence of weather and climate on healthy man can no longer be denied. Although some of the experiments described may require further confirmation, the majority of the studies confirm the important conclusion that the living body is continually subjected to the meteorological environment in which it lives. Despite the homeostatic properties of the human body, considerable changes in the internal environment can be brought about, which may lead to disease if the normal physiological processes are near the morbidity limit of the organism.

Section 3. Acclimatization (Acclimatization Biometeorology*)

Subsect. A. GENERAL PHYSIOLOGICAL MECHANISMS OF ACCLIMATIZATION

by

W. V. MACFARLANE

1. Introduction

Heat and cold are subjective categories (see p. 33) within the physical continuum of energy levels lying between —273° C and the temperature of new stars. Man survives in only a small part of that range, between about —60 and +60° C. Within those limits, environments between 21° and 26° C are judged comfortable by man clothed and at rest (Fig. 73). Thermal comfort or survival depend upon the energy balance of the organism regulated by alterations of heat production and heat loss (see p. 208).

As a homoiotherm, man is provided with a thermostatically regulated internal environment (see p. 232), and the thermal properties of the body are largely those of water, which is a useful thermostatic fluid comprising 55–70% of the body mass. Henderson and later Barbour[1426] pointed out that the physical behaviour of water made it suitable (specific heat 1.0) for heat

* A brief summary of general principles was already given on p. 241.

storage, as a slow-changing thermostatic fluid; for heat transport in the milieu intérieur, and for cooling by evaporation (latent heat of evaporation 539 cal/g). The freezing point of water is below the body temperature of survival for mammals in ordinary circumstances, though in experimental hypothermia (Smith[1559]), rat or hamster cells may be reversibly frozen if not more than 50% of the body water becomes ice and if the temperature change is rapid. When sperm are frozen, dehydration is necessary to assure functional recovery. Water in extreme cold is not the ideal fluid, and when it freezes, cellular processes are disrupted by the removal of available water as ice forms in cells.

The physiological mechanism of the human thermostat was already discussed by Tromp in a previous section (pp. 208). Glaser and Newling[1469], who discussed the thermostatic aspects of man, pointed out that the thermal balance is not constant, but varies from day to day and hour to hour, even at rest.

In operational terms "heat" may be regarded as a sensation and a judgement registered when the control system switches to increase the cooling of the body and "cold" when it is turned in the other direction to preserve heat. For resting, clothed man, the relatively neutral zone of air temperature in which neither heating nor cooling predominates, lies between 20° and 28° C. For naked man the critical temperature of thermal balance (Scholander *et al.*[1555]) when no increase of metabolism is needed to maintain the heat content of the body, is about 28° C. Du Bois[1455] studying naked men in a calorimeter found that there was thermal balance between 28° and 32° C. The air temperature within a comfortable bed is in this range, though 31° to 33° C is more likely to be comfortable than the lower part of this range (Macfarlane[1510]). As the gradient between a mean skin temperature of 32° C and the outside (room) air increases, more blankets are added to maintain bed air at about 32° C.

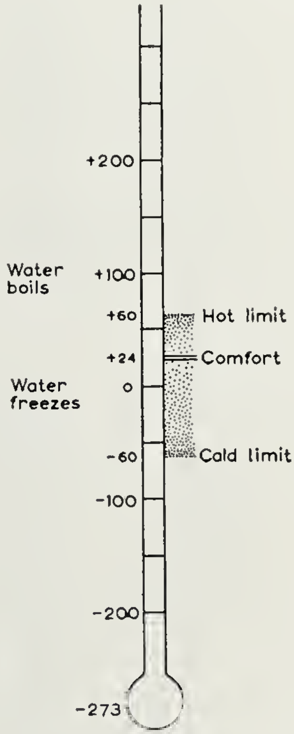


Fig. 73.
Man can survive between —60° and +60°C, but he is comfortable when lightly clothed and at rest, only in a narrow temperature range between 21° and 26° C. At the extremes of temperature elaborate protection is necessary to ensure survival (after Macfarlane).

Comfort (see p. 230) is a feeling state experienced when there is little need

TABLE 30

Physiological factors	*Observed meteorotropic phenomena*	*Authors and reference numbers*
BLOOD, *cells*		
leucocytes	Increase after steep barometric fall (Wigand, Alvarez). Decrease after foehn, after previous intracutaneous injection of NaCl (Mörikofer, Stahel). Increased adhesion (von Philipsborn). Max. Oct.–Febr. (Lambin and Gerard); max. April, min. August (Tromp)	Alvarez[1227], Lambin and Gerard[1228], Mörikofer and Stahel[1229], von Philipsborn[1231], Wigand[1233], Tromp[549]
eosinophils	Increase from winter to spring, normal in summer	Romeyke (see de Rudder [6, p. 217])
erythrocytes, specific gravity	Seems to rise in summer	Watanabe[1250]
erythrocytes, packed volume	Max. Febr.–March, min. in July and Aug. in Japan (Watanabe)	Watanabe[1249]
BLOOD, *serum*		
protein spectrum	Total serum protein decreases in summer (Depner, Tromp). Albumin level high in winter, low in summer (Tromp). γ-Globulin usually high in summer, low in winter (Tromp)	Depner[1238], Levin *et al.*[1202], Mehrotra *et al.*[1239], Riggs *et al.*[1241], Tromp[549]
calcium level	Min. in Febr.-March (8.5 mg/100 cc), max. in Aug. (11 mg/100 cc)	Bakwin *et al.*[1255], Drescher[1256], Kuroda *et al.*[1257]
magnesium level	In Japan min. in Febr. (2.12 mg), max. in Dec. (2.85 mg)	Allcroft *et al.*[1261–1262], Bartlett *et al.*[1263] Duncan *et al.*[1264], Hasselman[1265], Krehl [1266], Kruse *et al.*[1267], Kuroda *et al.*[1268] Riedesel *et al.*[1269]
phosphate level	Min. in Febr., max. in summer and autumn (average level 3–5 mg/100 cc)	Grassheim and Lukas[1258], Hess and Lundagen[1259], Williams[1260]
vit. C content	Low in winter, high in summer. Ascorbic acid inhibits hypertrophy of adrenal gland during cold	Dugal *et al.*[1270], Raoul *et al.*[1271], Trier[1272]

	(12.85 γ)	Fenger[1275], Kendall *et al.*[1277], Nitzescu and Binder[1278], Seidell[1279], Veil and Sturm[1280]
fibrinolytic properties	Bloodclotting time very low shortly before cold front passage (Caroli and Pichotka). After cold front passage strong fibrinolysis (Caroli)	Caroli[1242], Halse and Lossnitzer[1243]
opsonine-alexine and diphteria anti-toxin content	Diphteria anti-toxin titer decreased during cold season and after cold fronts	Wildführ[1370–1373]
isohemagglutinin content	Strong decrease of β-isohemagglutinin after sudden weather changes	Welcker[1374], Wildführ[1375]
BLOOD, *miscellaneous*		
volume	Increases with heat stress, decreases with cold (coldfronts, polar air)	Bazett *et al.*[1244], Bianca[1245], Burton *et al.*[1246], Forbes *et al.*[1247], Maxfield *et al.*[1248]
haemoglobin	After heat stress increased plasma volume, decreased Hb; after cold stress increased Hb (Bass *et al.*). Hb lower in summer than in winter (Coulthard, Depner, Tromp). On sea-trip from Liverpool to Peru decreasing (Barcroft)	Bass *et al.*[1212], Bratt[1215], Coulthard[1216], Cullen[1217], Depner[1218], Engelbreth *et al.*[1220], Finsen[1221], Friedländer *et al.*[1222], Henderson[1224], Oerum[1225] and others
prothrombin	Min. in children (in Hungary) between Sept.–Dec. (Banos). Fluctuation in prothrombin index with airmass and B.P. changes (Halse, Quennet)	Banos[1234], Halse and Quennet[1235], Rodahl[1236]
oxygen capacity	Increases from Jan.–May (in children < 6 y.), from Febr.–Aug. (in older children) (Nylin)	Nylin[1251], Straub *et al.*[1252]
carbon dioxide capacity	Max. abs. of blood around 21 Dec., min. around 21 June	Nylin[1253], Straub *et al.*[1254]
sedimentation rate	Usually low in winter, high in summer (Tromp). Short term fluctuations: low B.S.R. values after influx of cold polar air (Tromp)	Franke[1282], Giordano[1283–1286], Jores and Strutz[1287], Rodahl[1288–1289], Sugita[1291], Tromp[549]
coagulation	Bloodclotting time particularly low shortly before cold front passage	Caroli and Pichotka[1296]
bleeding after treatment with anti-coagulants	Max. in Jan.–Febr., min. in July (Jordan)	Jordan[1297]

TABLE 30 (continued)

Physiological factors	*Observed meteorotropic phenomena*	*Authors and reference numbers*
HEART AND CIRCULATION		
diastolic blood pressure	High in wintermonths (part. Febr.), low in summer (Tromp)	Alvarez[1317], Betz[1318], Dietze[1319], Franke[1320], Hopmann[1321], Illenji[1322], Jaenisch[1323], Mörikofer[1229], Rodahl[1324], Sarre[1325], [1326], Spiro and Stähelin[1327], Tromp[1329]
angina pectoris	In W. Europe and Northern U.S.A. max. in Jan.–Febr., min. in July–August	Amelung[2394-2395], Bartels[2397], Bean[2399], Fladung[2406], Heyer[2408], Kisch[2411], Kolisko[2412], Mills[2415], Stocks[2419], Ströder[2420], Teng[2421], Tromp[2422], Weiss[2424], Wood[2425]
myocardial infarction and coronary thrombosis	In W. Europe and Northern U.S.A. max. in Jan.–Febr., min. in July–August	
apoplexy	In W. Europe and Northern U.S.A. max. in Jan.–Febr., min. in July–August	Tromp[2422]
post-operative embolism and thrombosis	Increased embolism during days with front passages (both cold and warm)	Andresen[2968], Bartsch[2969], Domrich[2978-2979], Kayser[2985-2986], Kümmel[2988], Lampert[2989], Maurer[2990], Merck[2991], Sandritter[2997], Stumpfegger[3002], Raettig[2992], Rappert[2993-2994] *et al.*
RESPIRATORY SYSTEM		
bronchial asthma	Min. in Jan.–Febr., max. Aug.–Oct.	Schook and Tromp[1918a]
SKIN		
capillary resistance	Increasing after cold fronts, decreasing after warm front	Arimatsu[1377], Regli and Stämpfli[1378], Wyss and Gianoli[1379]
dermographic skin capillary test	Capillary structure of the skin changes rapidly in spring; excitability of peripheral nerves in skin increases as shown by dermographic tests	Bettman[1380-1381], Franke[1382], Jungmann[1383], Kanz *et al.*[1384], Nothhaas[1385]
electrophoretic adrenaline and acetylcholine	Acetylcholine test shows earlier the influence of cold front passages (8 h. and more) than adrenaline tests	Becker *et al.*[1386], Scholz[1387], Straube *et al.*[1388]

direct current resistivity*	Very high during falling barometric pressure and foehn (Dugge)	Dugge
MUSCLES		
metabolism	Phosphoric acid and glycogen content of muscles of rabbits high with cold fronts, low with foehn and warm fronts	Riesser and Kunze[1392–1394]
strength	Changing during different weather conditions	Dexter[1395]
chronaxy of motor nerves	Influence of ionized air on chronaxy (*i.e.* the minimum time at which an electric current, just twice the rheobase value, will cause contraction; *rheobase* is the minimum potential of electric current necessary to stimulate)	Edström[1396]
ENDOCRINAL SYSTEM		
iodine content of thyroid	Min. in Dec.–April, max. in July–Aug.	Kendall and Simonsen[1345], Seidell and Fenger[1351] and many others
general activity of thyroid	Increased thyrotrophin production and general activity after cold stress followed by temporary hyperthyroidism. After continued cold stress effect becomes less and less (Leblond)	Baillif[1336], Cramer[1339], Uotila[1354–1359] and many others
iodine content of organs	In dogs max. in March (Sturm, Buchholz)	Sturm and Buchholz[1352], Veil[1359], Nitzescu and Binder[1348]
URINARY SYSTEM		
diuresis	Decreasing after heat stress, increasing during fall in temperature (cold front, polar air influxes)	Fuchs[1307], Helbig[1308], Strassburger[1309], Tromp[305]
17-ketosteroid secretion in urine	Increase after coldstress (cold fronts, polar airmasses), decrease with increasing temperature. During very strong heat stress also increasing	Morinaga[1302], Tromp[549], Zimmerman *et al.*[1304]

* After emotional conditions often a sudden decrease in the direct-current skin resistivity is observed, known as *psychogalvanic reflex*, a phenomenon related to sweat gland activity. Alternating current tests have shown that not a true resistivity change occurs but only a change in the recorded electromotoric forces in the skin. The observed e.m.f. is the balance of the e.m.f. created by the current and the counter e.m.f. created by the brain cortex in the peripheral nerves. During stress conditions this counter e.m.f. is high, therefore the observed e.m.f. is small. As the current $i =$ e.m.f./resistivity with constant i the apparently small e.m.f. gives the impression of being caused by an increased resistivity and *vice versa*. During sleep the skin resistance is usually very high.

TABLE 30 (continued)

Physiological factors	*Observed meteorogropic phenomena*	*Authors and reference numbers*
EYE		
acute glaucoma	Particularly frequent after cold front passages	Bauer[2298], Brückner[2301-2302], Cuendet [2305], Fischer[2307], Geissler[2308], Hell[2309], Huerkamp[2310], Koike[2315], Lobo[2316], Maynard[2318], Sauter[2324], Schorn[2326], Steindorf[2327], Streiff *et al.*[2296]
retinal detachments	Max. in June, min. during winter	Jonkers[2311-2312]
MISCELLANEOUS		
growth	In children slow in winter, rapidly increasing in spring	Nylin[1332]
weight increase	In children max. Sept.–Nov.	Nylin[1333]
standard metabolism	In children max. during autumn. General metabolism decreasing sharply during winter. In diabetics during late spring, summer and early autumn higher metabolism. In winter low metabolism, high blood sugar content, high insuline consumption (Chrometzka)	Chrometzka[1311], Fuchs[1312], Hughes[1313], Nitschke[1314], Nylin[1315], Sargent[1316]
pharmacological sensitivity	Tincture of digitalis more toxic during steeply falling barometric pressure (Macht); toxicity of morphine sulphate highest during cold front passages, great atmospheric turbulence, etc. (Nedzel, Sargent)	Findeisen[3405], Macht[3408], Nedzel[3410], Ossoinig[3412], Petersen[3413], Sargent[3415]
permeability of tissues	After cold fronts decreasing, after warm fronts or foehn increasing	Lotmar and Häfelin[1376]
bacteria	Daily variations in number of streptococci on mucous membrane in relation to environmental temp., etc.	Sundermann and Baufeld[1397]
inorganic chemical reactions	Variations in stability of colloids	Bortels[1398], Findeisen[1399], Piccardi[1402-1409]
	Changes in crystallisation pattern of undercooled solutions	Pfeiffer[1415]
nitrogen and phosphoric acid secretion	High during cold front passages	Fischer[1369]

to regulate heat flux in order to maintain body temperature; but rigid prescription of comfort zones is not possible because of individual behaviour, tastes and reactions. Body temperature is also difficult to define (see p. 221) since a living body has different temperatures according to age, activity, time of the day, posture and region of the body measured (Cranston *et al.*[1448]). Maintenance of relative constancy of the human rectal temperature between the average 3 a.m. minimum of 36° and the 5 p.m. maximum of 37.4° C (Pickering[1540]) requires regulatory work which increases in environments outside the neutral zone. The average rectal temperature of adult residents of Singapore was found, for instance, to be 0.25° C higher than that of similar subjects in England, the mean air temperature difference between the environments being 9° C (Adam and Ferres[1418]). Anyone spending 2–3 hours each day in an environment below 20° or above 28° C makes emergent heat control adjustments, and after 2 to 3 weeks, changes of body function are established which persist for 2 or more weeks after return to a neutral temperature. The slowly achieved changes comprise acclimatization. In this concept of acclimatization, animal functions are regarded as being sufficiently plastic and elastic in character to cope with the environment. The altered functions will usually benefit work or efficiency. There are limits, however, beyond which reactions to severe climates reduce function and lead to disease. Acclimatization is a reversible set of events with no damage to the organism. Disease is less reversible, and involves some destruction.

2. *Terms and Definitions*

A variety of terms has been used in describing modifications of function to meet the environment. In English the word "acclimatization" seems to have come into use about 1830 to describe the adjustment of plants and animals to new habitats and different climates. The following definitions seem useful:

Acclimatization is the complex of reversible changes of physiological response which increase the efficiency of individual organisms while they remain in an environment outside the neutral zone.

Acclimation may denote the long-term changes taking place during a life time (Burton and Edholm[1439]). Acclimation has also been used by Prosser[1541] to describe the phenotypic adjustment of animals to immediate stimuli; or the day to day changes in systemic and cellular organisation. Until a standard usage is accepted, it seems better to regard acclimation as a synonym for acclimatization. It is a term not commonly used.

Habituation is the alteration of reflexes, responses or percepts as a result of retained central nervous experience of specific stimuli. It may be reduced by chlorpromazine (Glaser and Lee[1468]).

Adaptation has two connotations: (a) Biologically it is used to generalize the concept of evolutionary adjustment of species over many generations, as mutations are selected by environmental stresses. (b) Physiologically, adaptation connotes the rapid changes of cellular function brought about by continued stimuli. The term applies mainly to nerves and receptors. Often adaptation is used, however, as a synonym for acclimatization.

3. *Early Acclimatization Studies*

The Hippocratic awareness of the effects on men of airs, waters and places; the personal experience of travellers from polar to equatorial latitudes; or the more modern ascent to mountains (with mountain sickness) and colonisation of new lands, all provided evidence of some differences of human efficiency in unfamiliar climates and of slow adjustment of men to new temperatures. Robert Boyle[1435] recorded artificial acclimatization of animals in his pneumatic machine. He was able to show that they became accustomed to rarefaction of the air and suffered less on successive exposures to low pressure. Attempts at quantitative study of these events, however, are less than a century old. Some of the early work is recorded vividly by Paul Bert[1433] in his account of adaptations to altitude. As people from temperate zones moved to the arctic or to the tropics (particularly since the 16th century), it became clear that some adjusted well, and others failed to reach a useful working status.

By 1921, Barbour[1426] could give some account of this process in man exposed to tropical types of climate. From that time groups in U.S.A., Britain and Germany began seriously to try to measure the subjectively realised differences between the hardened old-timer and the new-comer to difficult environments. Eijkman at the end of last century and Radsma[1542] in the past 30 years gathered evidence of metabolic and physiological changes in Europeans living in Java. Young *et al.*[1588] and Sundstroem[1567] sought seasonal differences in the blood chemistry of Europeans living on 19° S in Australia and compared them with temperate zone values. Although some differences appeared (such as low urinary chloride) no clear mechanism was detected, largely because most of the tests used and parameters measured were not those that alter with climate. Sundstroem suggested however, that the adrenal might be exhausted in the heat.

When Barcroft and his party[1428] made their journey to the Andes from Europe, they recorded an increase in blood volume proportional to the ambient temperature. In a similar fashion, Martin[1528] passing from Australia to Britain detected a series of changes in his basal metabolic rate (B.M.R.) which decreased near the equator. The clearly stated findings of Barcroft and Martin have been followed by more numerous estimations. Exposure to heat and cold have subsequently been claimed either to have little or no effect on blood volume or B.M.R., or to produce dramatic changes (Bass *et al.*[1430]).

From these origins, a physiology of differences in function has grown, as the counterpart of physiological studies of mechanisms (such as conduction, transmission or digestion). The differences in function produced by age, heat, cold, altitude, work or disease are not changes in one system but involve the whole body, as one unit. A new steady state is reached by both the tissue fluids and the cells. Barcroft[1427] saw "each adaptation as an integration", while about the same time Henderson came to look upon "adaptation as a new physicochemical equilibrium state". Although this type of physiology concerns the whole organism, there are usually some major adjustments, such as water and sodium loss during sweating, upon which depend many other changes of nervous, vascular, renal and endocrine origin.

4. Main Features of Acclimatization

In acclimatization there are three main components:

(1) Detection by the body of changes in the surroundings. The skin and nervous system combine as the sensing elements.

(2) Fast reaction by the body, by vascular, sweating or shivering responses through the nervous system.

(3) Slower endocrine changes, modified cellular metabolism and adjustments of behaviour and judgement. These subtle changes are not yet analysed.

In hot climates, man decreases insulation and increases the rate of turnover of water and to a lesser degree, of salt. In cold regions, there is a greater turnover of chemical energy together with an increase of insulation. Other modifications depend upon these primary changes. Acclimatization is mostly reached within one week, but some 2 or 3 weeks are required to approach a steady state. Reversal of the changes is slow, and acclimatization to heat survives 2 weeks in the cold. Some adaptations, particularly of behaviour and attitudes are not achieved until years have passed, or they may require a new generation.

Acclimatization to heat

In adults, acclimatization to heat is associated with the following features: (*i*) Increased ability to work and maintain skill with progressively less cardiovascular strain (lower pulse rate and cardiac output); (*ii*) Increased volumes of sweat, which appear at a lower body temperature; (*iii*) Decreased urinary and sweat sodium and solute content, if the diet contains less than about 15 g/day of sodium chloride. Secretion of aldosterone; (*iv*) Increased plasma and "extracellular" fluid volumes; (*v*) Increased ability to eat and sleep in the heat; (*vi*) Reduced metabolic rate at rest, and reduced excretion of metabolic products of adrenal steroids; (*vii*) Neuronal facilitation of blood vessel and sweat gland control, with central nervous habituation at both conscious and regulatory levels.

Acclimatization to cold

This involves five mechanisms: (*i*) Increased production of heat by shivering, muscular activity or tissue metabolism; (*ii*) Peripheral vasoconstriction with sufficient blood flow in the extremities to allow them to remain efficient; (*iii*) Decreased "extracellular" fluid; (*iv*) Increased thyroid and adrenal cortical hormone production, initially, at least; (*v*) Central nervous habituation.

Acclimatization to one form of stress does not confer resistance to other disturbances. There is not cross-acclimatization between heat and cold, or altitude and exercise. It will be convenient, therefore, to consider first the thermal balance of the body, then the events that take place when adults pass from a neutral to a hot climate. These may be compared with those found on passing into a cold region.

The meagre knowledge of the reactions of children to temperature will be considered separately.

Subsect. B. THERMAL BALANCE

by

W. V. MACFARLANE*

1. *Equations of Heat Transfer*

The body is a physical system normally in balance with the environment. It may be conveniently considered to be a core surrounded by a shell where vasomotor control can influence heat transfer. Across the shell of skin, heat

* Although these various processes were already discussed by Tromp on p. 208, in the present section certain aspects will be discussed in greater detail.

transfer for different layers lies between 20 and 60 cal/cm/sec/°C · 10^{-5} (Vere[1574]). Air temperature, air movement, humidity and radiation determin heat flux at the surface (see also the formula of Molnar, p. 246). The transfer may be summarized as

$$H = \frac{K\,(t_s - t_a)}{I_a + I_c}$$

where H = rate of heat loss from skin, t_s = skin surface temperature in °C, t_a = ambient air temperature in °C, I_a = resistivity of air to heat passage outward, I_c = resistivity of clothing to heat loss, K = 5.5 kcal/m²/h; I = "*clo*", a unit of insulation defined as 1 clo = 0.8 $\frac{°\mathrm{C}}{\mathrm{kcal/m^2/h}}$ and it represents the amount of insulation that will maintain a sitting man whose metabolism is 50 kcal/m²/h comfortable at 21° C, in air of less than 50% relative humidity and 6 m/min movement (Gagge *et al.*[1465]).

The "*met*" is a unit of heat production also introduced by Gagge *et al.* It represents the calories produced by a man sitting in a room at 21° C with a mean skin temperature of 32° C and heat production of 50 kcal/m²/h.

The above equation indicates that heat loss is proportional to the temperature gradient between skin and air, and inversely proportional to insulation. The insulation is provided by both the shell of the body and by clothing. Clothing is effective largely because of the air it contains, since air has a much lower thermal conductivity (6 cal/cm²/sec/°C · 10^{-5}) than cellulose fibres (30) or wool. On the other hand, for fine fibres the bulk density is a minor factor in insulation, provided that air makes up about 90% of the volume. Fur, fleece, air and clothing all have an insulating value of 1.8 – 1.9 clo/cm (for further details see p. 34).

If there is strong convection from wind, the insulation of clothing is ineffective. Wind effects were discussed by Tromp on pp. 43 and 225.

Radiation gained from the sun has its greatest intensity in the shorter wavelength region from about 2800 to 20,000 Å (2μ). There is about 30% more reflection of wavelengths less than 1μ by white than by black skin, but radiation of longer wavelengths is equally absorbed by all shades of human skin (Hardy and Muschenheim[1474]). For anyone in the open, radiant energy can be a major source of heat, especially in deserts (where there is little shade and both sun and soil radiate), on snow or on water. The insolated area of man is equal to the size of the shadow cast and this varies with posture and time of day as well as with latitude. The sun yields about 1.2 cal/cm²/sec at ground level.

Radiant energy loss from the body is by long infrared radiation (see

p. 36) which reaches its greatest intensity at 9μ wavelength. Negro and white skins are equally black as radiant sources for wavelengths of 1μ or longer. The obverse of radiant energy gain from hot objects or the sun, is radiant loss to cool surfaces. A window cooled by an outside winter temperature acts as a sink for radiation from persons inside (see p. 37). It may be felt as cold if its temperature is below that of the skin.

The other form of physical regulation is by evaporation (see p. 37). Burch[1436] estimated that at rest in air at 21° C, 5.8% of the heat loss of the human body was by evaporation of water from the alveoli, and 3.6% was lost by carbon dioxide vaporization. Evaporation from the respiratory tract is not important in man as a means of losing heat. Insensible water loss through the skin is similarly not changed singficantly by a hot climate (Newburgh and Johnston[1532]). The effectiveness of sweating depends upon the relative vapour pressure of water in the air and of the sweat, as well as on the wetted area. When sweat becomes hot it exerts a higher vapour pressure. As salt becomes concentrated in sweat, its vapour pressure falls (Macpherson and Newling[1522]) so evaporation in a humid climate may be small, unless sweat drips off carrying away salt. Sweating is most effective for cooling in low humidities and high temperatures amongst acclimatized people who secrete little salt in the sweat. Convection (up to 60 m/min.) of air below 37° C increases cooling, by preventing the local saturation of the surrounding proprioclimate, which is also within the clothes. Unless sweat is evaporated by taking heat from the blood and skin, it provides no cooling. Evaporative cooling may be generalized as

$$H = \frac{K_e\,(P_s - P_a)}{r_a + r_c}$$

where H = heat loss by evaporation, K_e = 5 kcal/m²/h (evaporative constant), P_s = vapour passage of skin in mm Hg, P_a = vapour passage of air in mm Hg, r_a = resistivity of air to vapour passage and r_s = resistivity of clothing to vapour passage.

Women sweat less than men, at a given environmental temperature. They appear (Hardy *et al.*[1476]) to reduce metabolic rates by 15% on being heated, whereas men maintain the same B.M.R. Heat loss by women in the cold is also reduced by more adequate insulation.

The problems of thermal balance are treated in detail by Machle and Hatch[1518], Winslow and Herrington[1583], Burton and Edholm[1439] and by Lee[1501]. A steady state, with some oscillation, can be maintained in health over about 80° C range of environmental temperature. Comfort is achieved, however, when the input and output of heat are almost equal.

2. *Thermal Comfort*

Comfort zones for clothed adult subjects at rest in the shade have been described for human groups in many parts of the world. In Table 31 some of the findings are shown, using the dry bulb temperature or effective temperature as the index of the environment, and subjective votes as the index of response. Inhabitants of cold zones prefer lower temperatures than those acceptable to tropical groups. Outdoor workers in Australia remain comfortable in hotter climates than indoor workers. There is a wide range of taste in any population, and it is likely that both acclimatization and genetic influences determine whether heat is tolerated. Migrants to the tropics fall into two groups: those who are uncomfortable but persist, and those who are too uncomfortable to remain there. Life in the tropics requires a change of comfort judgements, and a considerable section of Europeans can make the adjustment. There is much to be said for the suggestion (Scholander *et al.*[1555]) that man was originally a tropical animal.

Index temperatures have been derived from combination of subjective response and physical measurements of air temperature, movement, humidity and radiation. The *effective temperature* (E.T.) was derived from the comparison by human subjects in the U.S.A. of a given environment with a saturated still atmosphere (see p. 41). Although radiation was ignored, the E.T. has been useful. It still, in spite of correction, weights humidity too heavily, however, and it is not strictly applicable to tropical people. Bedford[1432] usefully employs the corrected E.T., in which globe thermometer readings replace dry bulb temperature.

Many environmental studies have been made with E.T. as the reference temperature. It is better, however, to have separate records of wet and dry bulb temperatures and air movement, rather than the derived index, when comparing climates or responses, since responses are not necessarily the same in all environments amongst all human groups.

Geographically, the minimum temperatures encountered increase by about 8° C for each 10° latitude moved towards the equator, but there is a fall of 5.8° C for each 1000 m altitude above sea level (Lee[1500]).

Subsect. C. THERMAL IMBALANCE

by

W. V. MACFARLANE

1. *Acclimatization to Heat*

General concepts

Heat strain is the response of the body to increased heat content, and it

TABLE 31

COMFORT ZONES FOR CLOTHED ADULT SUBJECTS AT REST IN THE SHADE, DESCRIBED FOR HUMAN GROUPS IN DIFFERENT PARTS OF THE WORLD

	England	*U.S.A.*		*Australia*		*India*	*Java*	*Singapore and Malaya*	
Latitude (approx.)	52°	40°	30°	35°		20°	5°	2°	
Race	European	European		European		Indian	Indonesian	European	Malay Chinese
		N	S	outdoor	office				
Dry bulb T C comfort range	15.5–20	21–27	22–29.5	21–30.5	22–28	22–29	22–29.5	24.5–29.5	26.5–30
Effective T C comfort range	14–19	19.5–22	20.5–24.5	20–26	20–24.5	21–26.5	20–26	23–25.5	21–26.5
Reference	Bedford[1432]	ASHAE[1125]		Macfarlane[1510]		Malhotra[1524]	Mom[1530]	Ellis[1458]	Webb[1578]

Range of shade temperatures found comfortable by clothed adults at rest. The estimates, derived from comfort votes and conventions, differ somewhat amongst the authors. Dry bulb temperatures are in some cases estimates since only effective temperatures were reported.

Tropical peoples prefer higher temperatures than temperate zone groups. The most comfortable temperature lies about the middle of each range given.

leads to cooling, so that a new balance is obtained. Most of the discussion to follow will concern the strain reactions of man.

Receptors. The skin is provided with nerve endings sensitive to temperature change. It is not certain that Ruffini endings are the only devices responding to heat (see p. 210). It is, however, likely that sensory end organs have optimum temperatures of activation, some between 39°–40° C for instance, others at 35°–36° C, and others (recording cold) at 25°–28° C. For a given heat receptor to discharge the energy change at the skin surface is small — of the order of 0.00015 cal/cm²/sec over 200 cm² (Hardy and Oppel[1475]). A rise of 0.3° C in skin temperature is perceived and large areas detect smaller amounts of energy than small skin zones. Further details were described in previous sections (p. 210).

"Temperature regulation centres" have been fully described on pp. 232–241.

Nervous control

Heat and cold differ in their central triggering mechanisms. Pickering [672] observed that heating a limb with its circulation occluded produced no reflex changes. When the blood was permitted to flow from the limb to the brain, vasodilation and sweating were initiated. On the other hand, Kerslake and Cooper[1487] produced widespread reflex vasodilation and sweating of limbs by radiation of the skin of the abdomen. Similarly there is an oro-oesophageal reflex set up by swallowing fluid—or by peppers (Glaser and Lee[1468]) to produce sweating.

A combination of hypothalamic and peripheral effects seems to underlie the regulation of heat transfer above 28° C air temperature.

Discharge of cells in the cooling region brings into action neurones of the cardiovascular and sudomotor zones of the medulla. The vasomotor activity is widespread, though there is a spatial and temporal sequence of activation. Local conditioning of neurones in the reflex arcs has been demonstrated by Glaser and Whittow[1170]. By immersing the left arm in cold water, vasomotor responses were elicited. The extent of the rise of blood pressure became less with acclimatization to the procedure (see p. 241). When the right arm, however, was subjected to cold, a new rise of blood pressure was obtained, equal to that originally elicited from the left arm. This may be interpreted as a unilateral learning or habituation of neurones. In acclimatization there is further modification of the reflex pattern so that more sweating occurs for a given heat load than in non-acclimatized subjects.

(a) Cardiovascular

In air above 28° C there is first dilatation of the arterioles and capillaries of the face. This is followed by increased blood flow in the skin of the hands and trunk. Finally the vessels of the skin of the feet become fully dilated. These mechanisms are activated by three means: (*i*) increase of the heat content of the body by metabolism or exercise, (*ii*) conduction of heat from warmed air or ingestion of warm fluids, and (*iii*) radiation. Gerbrandy *et al.*[1467] found that 2–3 kcal applied as a warm intravenous infusion induced vasodilatation at rest. The insulation of the body shell is reduced by vasodilatation and heat is brought to the surface to be removed by evaporative cooling, conduction and radiation. In the feet and hands there is release of vasoconstriction. In the forearm Edholm *et al.*[1456] found evidence for reflex vasodilatation which is not normally found in the extremities.

Blood pressure. Several observers (Radsma[1542], [1543] Burch and Hyman[1438]) have reported a fall in systolic and diastolic blood pressure of about 5 mm Hg. The change is small and presumably results from vasodilatation in the skin, which is not completely compensated by increased plasma volume and cardiac output.

Heart work. The early estimate of Scott *et al.*[1940] that cardiac output increased on exposure to heat has been followed up by Burch[1438] who measured the work of the human heart in New Orleans during summer at 35° C with high humidity. He found increase in heart rate, in cardiac output (by about 40%) and in the rate of working of the myocardium when heat load increased. Dry heat, at 37°, on the other hand, seemed to have little effect on heart work other than to reduce it, when the subjects were sedated (Sancetta *et al.*[1552]). During heating, perfusion pressure must be maintained in a larger vascular bed. This is assisted by the increase in blood volume in a hot climate, but it is counteracted by greater laxity of heated veins (Wood and Bass[1584]) in which blood pools on standing. Higher resting heart rates in the heat presumably have their origin in afferents from skin, carotid sinus and the right atrium, with reflex outflow passing down the sympathetic nerves to the heart. In other animals, such as ruminants, exposure to heat slows the heart although they have increased blood volume and skin dilatation. The reason for these differences is not clear.

(b) Sweating

Sweating by the eccrine glands (see p. 216) takes place by an ordered sequence of reflexes. Mostly these are concerned with evaporative cooling; but emotional sweating of face, hands and feet can occur in the cold. Sweating may be induced by pain, strong tastes, syncope or vomiting (Glaser and Lee[1468]). The order of recruitment of thermal sweating areas is first the dorsum of the feet, then calves, trunk, arms and last, the face (Randall *et al.*[1545]).

This is almost exactly the opposite order in which warmth is perceived, so that *thermal perception must be achieved through other fibres or means than those initiating sweating*. The amount of sweat is regulated by the number of glands brought into action. Both heat content of the body and skin receptors are involved in thermal sweating. If the core remains cool while the skin is heated, sweating will not begin.

The density of sweat glands is not uniform. There are about 200/cm^2 on the hand and arm, between 120 and 210/cm^2 on the forehead and trunk anteriorly, about 120/cm^2 on the leg and less than 40/cm^2 on the back (Randall[1544]). There are about 2 million sweat glands in man, and they function intermittently (Kuno[1491]). Under the influence of acetylcholine released by the sympathetic motor nerves supplying the glands, watery secretion is passed out to the surface for 2–10 seconds. A given gland then ceases to secrete for a similar period, while other glands go into action. The greater the stimulus, the more frequent the bursts of activity.

It is thought that there may be filtration of plasma into the base of the sweat gland with subsequent resorption of most of the dissolved substances. If, however, sweat is formed by subtraction of a watery fluid from the tissue fluid, with an osmolarity about 1/3 to 1/5 of that of plasma, the same amount of osmotic work would have to be done as in resorption. As a gland becomes fatigued (during high rates of sweating) the difference in concentration between plasma and sweat is reduced, which suggests failure of the glands to perform maximum work.

Composition of sweat (see p. 216). Sweat from eccrine glands contains electrolytes, some metabolites, and small amounts of vitamins and hormones (Robinson and Robinson[1550]). Changes in the concentration of the main constituents of sweat before and after a period of severe heating are shown in Table 32.

Acclimatization and sweat. Acclimatization to heat leads to a reduction of electrolyte and crystalloid concentration as well as to a greater volume of sweat (Bass *et al.*[1431]). Most of the change takes place within 7 days. Work in the heat increases the acclimatization and some degree of salt deficiency increases the extent to which sodium and chloride are reduced in the sweat, probably through the action of aldosterone.

Ladell[1494] found an increase in standard sweating from 545 to 865 ml in 60 min after 10 days in the heat, and there was a greater rate of sweating for a given rise of rectal temperature after 9 days heating. Using such tests he found that Nigerian natives were normally less acclimatized than Europeans could become in hot rooms in London.

Evaporation of sweat takes place when 560 cal/g are provided. At the

TABLE 32

SWEAT COMPOSITION BEFORE AND AFTER ACCLIMATIZATION OF MALE ADULTS

	Unacclimatized		*Acclimatized*	
	whole body sweat	*arm sweat*	*whole body sweat*	*arm sweat*
Bass et al.[1431]	*initially*		*14 days at 49° C*	
Vol./hour in ml	1084		1253	
K, mequiv./l	9–14		3–6	
Na, mequiv./l	120–138		50–70	
Na/K	10–13		12–17	
Cl, mequiv./l	125–135		50–70	
Creatinine, mg %	0.4–1.0		0.3–0.5	
Van Heyningen and Weiner[1573]	*initially*		*13 days at 46° C*	
Vol./hour in ml	606	20	1130	81
Cl, mequiv./l	44	114	60	66
Lactate, mequiv./l	9	24	8	12
Urea, mequiv./l	5.4	15	6	9
Pyruvate, mequiv./l	0.1–0.8			

There is evidence of a general reduction in solute concentration on acclimatization, although in Van Heyningen and Weiner's subjects, adequate salt replacement prevented a decline of choride in body sweat. There are regional differences in the concentrations found. Arm sweat is collected in a saturated atmosphere which may alter the sweat composition by raising the local skin temperature.

For the same heat stimulus a greater volume of sweat was produced on acclimatization.

skin surface, most of the energy comes from the skin, and indirectly from the heat of the blood. The thermal conductivity of water is many times greater than that of air, so the sweat is heated mainly from the tissues. In the sun, however, a fraction of the sweat on uncovered areas, would be evaported by absorption of radiation.

The rate of sweating in man varies with many factors, the chief of which are: (*i*) Blood temperature, raised by metabolism or external heat; (*ii*) Skin temperature: as this rises there is greater sweat flow and solute concentration; (*iii*) Duration of sweating: there is fatigue of the sweat glands after 2–3 hours; (*iv*) Acclimatization increases the amount of sweat from a given stimulus; (*v*) Age and sex: there is a decrease in relative sweat rate with increasing age; women sweat less in a given environment than men; (*vi*) Time of day: more sweat is produced during the afternoon than in the morning, at the same air temperature; (*vii*) Water replacement: there is some reduction in sweat rate when water loss is not made good (Ellis, Ferres and Lind in 1954).

Acute adjustments

(1) *Water and salt adjustment.* Sweating in man involves mainly loss of water and sodium chloride. In plasma there are 140 mequiv. Na to each litre of water; in sweat from 90 down to 25 mequiv./l. There is, therefore, more water loss from the extracellular fluid (relative to salt) by a factor of 2 in unacclimatized and by 5 in acclimatized people. The extracellular fluid loses water so that the Na should be relatively concentrated. In severe heat stress this has been reported to occur (Toor[1570]) with a rise of plasma Na to 180 mequiv./l. The possibility of a tropical hyperaldosteronism, with Na and water retention, should be examined. In the unacclimatized, this effect is less, since Na is lost in amounts closer to those found in plasma. Usually there is little change in plasma Na on sweating 2 to 3 l. For renal Na control see Wesson (in 1957).

(2) *Thirst and fluid replacement.* Fluid intake is to a large extent a routine of conditioned and social responses. When there is loss of fluid, however, thirst is experienced. This results in water seeking and drinking, and the nervous organisation of this pattern is mediated through the anterior hypothalamus (Andersson and McCann[1423]). The state of hydration of cells appears to be the driving force behind thirst during dehydration, rather than reduced extracellular volume. King[1488] in 1878 recorded the reaction of a troop of cavalrymen lost in the Llana Estacado of Texas for more than 3 days without water. "Although water was imbibed again and again even to repletion of the stomach, it did not assuage their insatiable thirst, thus demonstrating that the sense of thirst is located in the general system and that it could not be relieved until the remote tissues were supplied". This conclusion has been upheld in recent experimental studies, although the mouth and stomach probably act as satiation recorders in normal drinking patterns (Adolph[1420]) and much drinking is a conditioned response or social routine.

The thirst mechanism lags behind water loss so that after a day's work in which 8 l of sweat may have been produced, there is a deficit of 2 l of water even though thirst has been temporarily quenched. During the evening there is complete replacement. Thirst as such is thus an inaccurate measure of fluid status. This is particularly so when both water and salt have been lost in a ratio approaching that found in plasma, as in salt depletion dehydration.

The pattern of *thermal strain in man, working in the tropics,* may be illustrated from a field study. The complex of adjustments may then be regarded analytically as it is broken down in laboratory experiments.

The passage of an acclimatized man from moderate comfort on the 27° S latitude to the hot working environment of summer on 19° C, is illustrated in Fig. 74. Subjectively, the skin feels hot on going into an environment above 26° C, the face and feet provide more sensation of heat than other regions. Hands and feet usually feel turgid particularly after they have been in a dependent position. In the heat also, the heart beat is faster.

Water intake is proportional to the ambient air temperature, but exposure to sun adds to the heat gain and the water turnover. In a period of cooler

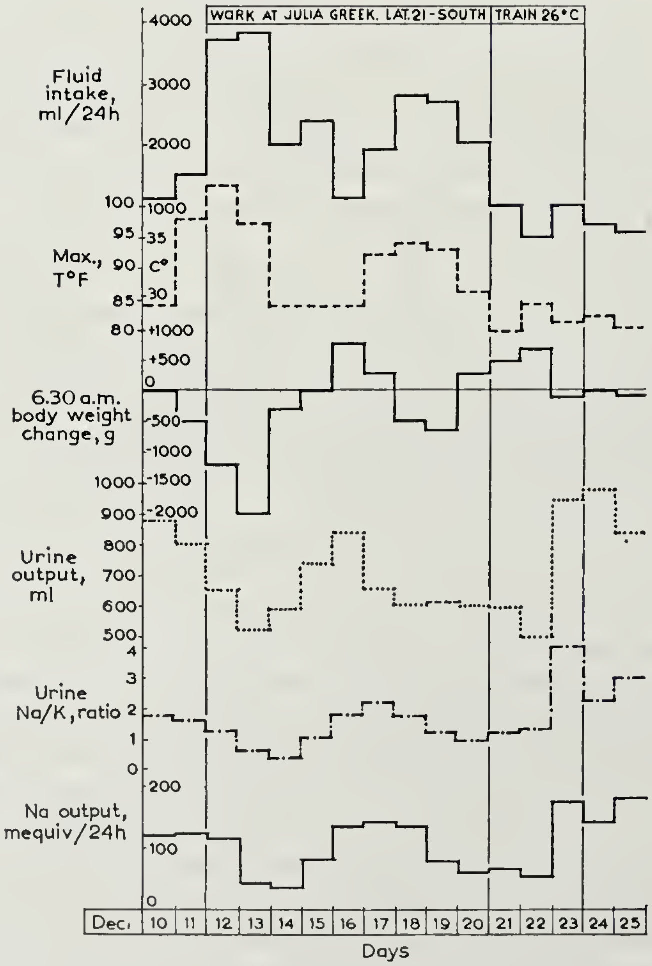


Fig. 74.
Water turnover and electrolyte excretion during sojourn in a hot region (1 adult subject). On moving from a warm to a hot environment, there was an increase of water intake proportional to the air temperature. Body weight, urine output, Na excretion and the Na/K ratio in urine changed reciprocally to air temperature as it rose or fell. On resting at 26°C there was a diuresis of Na and water after 48 hours (after Macfarlane).

weather with temperatures below 32° C, there is reduction of water intake, although this does not occur for 12 to 24 hours after the temperature falls.

Water intake is directly proportional to ambient temperature or thermal stress. Water and salt output through the kidneys are, however, inversely proportional to the heat load. Since the water intake is essentially a measure of sweating, urine output is the inverse of the amount of sweating that takes place. Day and night urine volumes are inversely related to temperature, but more water is lost at night than by day in the tropics. This diurnal ratio is the reverse of that found in temperate regions (Manchester[1526], Stanbury and Thomas[1562]) and it holds for work in the humid tropics (Macfarlane[1509]) as well as in the arid regions. The reduced urine flow takes 24 hours to increase towards its initial level, when conditions become cooler.

The ratio Na/K in the urine follows the same general course as the reduction in Na output per minute. More Na than K is of course being lost from the sweat.

On return to the cool environment (25° C or less) after one day of latency, there is a diuresis of Na, as well as of water. This lasts one or two days, and then the normal relations of water and salt turnover for a cooler environment are restored. The mechanisms underlying the changes illustrated in Fig. 74 may now be considered (see also p. 332).

(3) *Renal mechanism and hormones.* The reduction of water and sodium chloride excretion which occurs within 10–15 minutes of heating has complex origins. Posture is important. Merely changing from lying-down to standing-up results in reduction of urine flow and Na excretion (Fig. 75). Potassium is also excreted less rapidly in the vertical position. The origin of this immediate reduction appears to be neuro-vascular and there is evidence that adrenalin and noradrenalin produce the initial change of renal circulation leading to Na retention (Camp[1440]). The distribution of blood to the kidneys and its circulation amongst the tubules is also under nerve control. Wirz investigated and Schmidt-Nielsen[1553] has reviewed the concept of counter-current flow around the loop of Henle and the collecting ducts of kidneys in relation to water and electrolyte absorption. It is not proven that the primary adjustment to heat is a vascular redistribution in the kidney, but this seems to be the most likely explanation. It is inferred that pituitary anti-diuretic hormone (ADH) restricts water outflow (Camp *et al.*[1441]). It can be seen from Fig. 75, that there is very rapid and synchronous reduction of Na, K and water excretion. This effect follows the warming of the skin, particularly of the feet and hands with a resultant pooling of blood, and vascular reflex adjustments to this. Such reflexes probably arise in the right atrium.

The concept of volume receptors located in the region of the right atrium

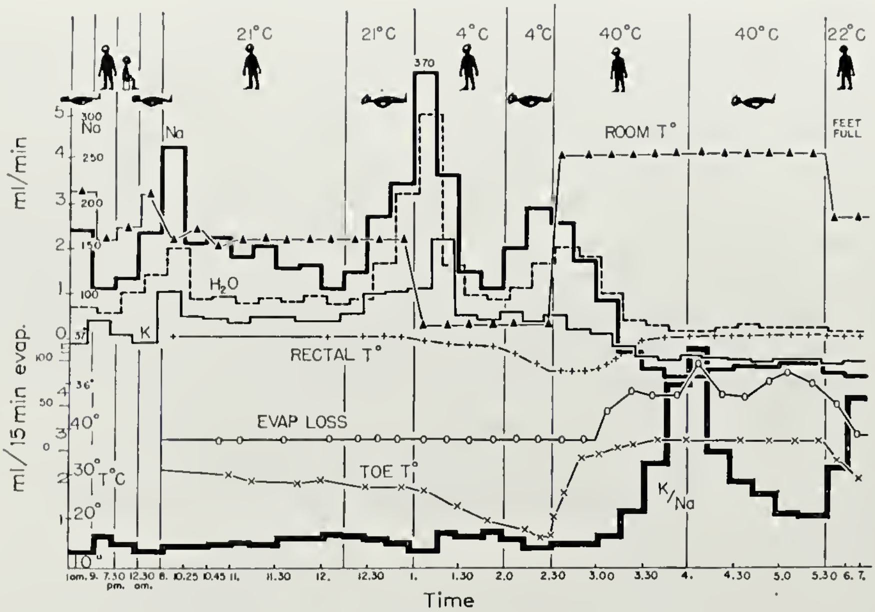


Fig. 75.

The effects of air temperature and posture on renal excretion of electrolytes and water. Standing at 21° C reduces Na, K and water excretion, but lying down produces a parallel increase in excretion of Na, K and water. Standing in a cold room at 4° C reduced these excretions after an initial high diuresis for 15 minutes. Lying down gave rise to a diuresis of Na and water. On entering an environment at 40° C there was no sweating while the rectal temperature remained low at 36.5° C, but Na, K and water excretion fell promptly. As the rectal temperature began to rise there was selective Na resorption and an increase in K/Na. This was reversed by lying down. Complex interactions of sympathetic nerves, adrenalin, aldosterone and ADH are involved in these changes (after Macfarlane).

is probably important here, and in the release of aldosterone from the adrenal cortex through a central mechanism. There is evidence (Newman *et al.*[1533], Farrell[1460]) that aldosterone can be released by afferent impulses impinging upon the hypothalamus which in turn releases a hormone to stimulate the adrenal cortex. The part played by aldosterone in Na retention during heating is still not clear, but during a period of sweating the excretion of aldosterone increases by ten fold or more (Falbriard *et al.*[1459], Macfarlane[1508], Collins *et al.*[1444]). This cannot be the whole answer, however, since intravenous injection of water-soluble aldosterone results in reduced Na excretion and a raised K/Na ratio in the urine only after about one hour (Fig. 76). After subjecting a man to heat, aldosterone is detectable in the urine after two hours (Macfarlane *et al.*[1517]). There is, however, a differential increase in Na resorption or decrease in Na excretion before that time. There is also reduced Na and water excretion before the onset of significant

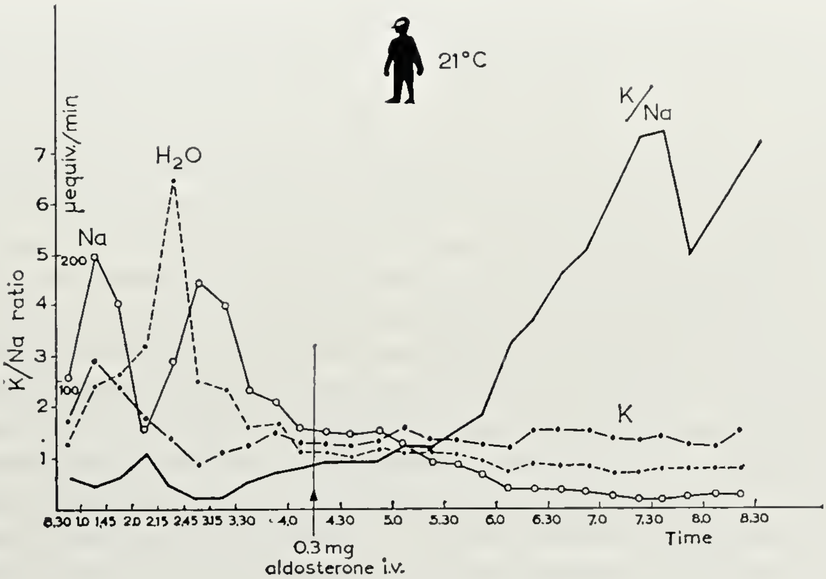


Fig. 76.
Effect of 0.3 mg aldosterone base (water soluble) intravenously on Na, K and water excretion in man. There was a delay of more than 45 minutes before Na resorption increased. Little change in the K or water excretion rate occurred (after Macfarlane).

sweating. In addition, there is a decrease in K excretion on heating, whereas under the action of aldosterone (Fig. 76) there is little change in K excretion, as Gowenlock *et al.*[1471] also report.

The most likely synthesis of these observations is that as heat impinges upon the skin and the blood temperature rises, there is vasodilatation with pooling of the blood peripherally. This leads reflexly to reduced water, Na and K excretion by adjustment of the kidney circulation. As sweat loss increases, Na and water are lost. A secondary and differential retention of Na in the kidney occurs due to fall in blood volume and aldosterone action (Farrell[1460]). Usually, as heating proceeds, it is found that the plasma volume changes are small, or in fact there may be an increase in plasma volume. This is particularly noted in the course of exercise, when plasma volumes increase.

Reduced water excretion occurs within 10 to 15 minutes on entering a hot environment. It seems likely that the initial reduction of water output results from the action of adrenalin and sympathetic nerves (Fig. 75). Later, as sweat is lost and dehydration begins, ADH may be detected in the plasma. Exposure of men at rest to 50° C produced little change in glomerular filtration or renal plasma flow in the experiments of Smith *et al.*[1560]. It is unlikely that changes in filtration, therefore, are primary in modifying Na, Ka and water excretion on acute exposure to heat. Exercise and dehydration lower both these aspects of renal function, however, possibly as a result of adrenalin secretion.

The part played by ADH has been discussed for some time (Hellmann and Weiner[1477]; see also p. 332). The observations of Macfarlane and Robinson in Australia indicate that there may be *increased amounts of ADH in the plasma during heavy sweating,* but these are delayed several hours and follow a time course quite different from the immediate reduction in urine flow on exposure to heat. Urine flow falls to less than 0.5 ml/min on exposure to 41° C within 30 minutes, during summer and winter. It is only during summer, however, and after at least two months of hot weather, that any reliable increase of ADH is found in the plasma. Even then, it does not usually appear until two hours of heating have passed, with the loss of 2 l or more of sweat (Macfarlane *et al.*[1517]). Plasma concentration commonly occurs on sweating in summer but not in winter. The urine flow is, however, reduced regardless of whether plasma concentrates or not. On exposure to heat the rate of urine flow falls to 0.2 ml/min and concentrations rise to over 1.2 osmols/l before ADH is detected in plasma. Yet injection of 1 unit of ADH by vein does not reduce urine flow below 0.5 ml/min nor is the concentration as great as on heating.

The administration of salt retaining hormones such as desoxycorticosterone can produce in sheep a condition in which there is concentration of plasma in winter. Since aldosterone appears during summer heating, it seems likely that there is some link between salt retention and the passage of water into and out of the plasma space. As sweating occurs, water leaves the interstitial space, but the plasma appears to maintain its volume differentially. In winter over 3 l of sweat may be lost from an adult man with neither decrease or increase in plasma volume. The exact mechanism is stil not clear.

The consequences of these observations are that, in contrast to the general assumption of most physiologists, *ADH cannot be considered as the major factor in prevention of water loss through the kidney during heating.* The primary water saving mechanism appears to have a basis in neurovascular adjustment. Adrenalin and sympathic nerve action probably combine in this. Later, with dehydrattion and concentration of the plasma, ADH increases, to help resist a diuresis, should water be taken.

The presence of ADH during dehydration may be of some assistance in preventing water replacement from disappearing in a diuresis. Certainly in sheep, dehydrated to 25% or more of their body weight, ADH is present to the extent of 150 μU/ml in the plasma. Within 30 minutes of taking a drink equal to 20% of the body weight, the plasma ADH disappears. A diuresis, however, does not begin at this stage. Diuresis takes place only after several more litres of water have been ingested. There are obviously some complex unknowns in this situation.

(4) *Influence of race.* There are reports of racial differences in excretion pattern in the tropics. Kenney[1486] found that the plasma urea concentration and the urea clearance of African Negroes were about half those of Europeans in the same region. The excretion of 17-ketosteroids by African natives (see p. 326) was found by Barnicot and Wolffson[1429] to be about half that of Europeans in the same region. A similar low excretion of 17-ketosteroids by Hindus is reported (Friedmann[1463]). The significance of these findings is not clear, although protein metabolism is probably involved.

(5) *Metabolic adjustments.* The early investigations by workers such as Eijkman and later Sundstroem[1567] sought the differences in overall metabolism, as well as nitrogen, sulphur, carbohydrate and mineral turnover. Few clear concepts emerged. It was apparent, however, that no major metabolic differences were involved in tropical living. One generalization that appears to be valid for endocrine responses to heat and cold is that the initial change is not fully maintained beyond about 2 weeks. Thyroid and adrenal corticoid activity is increased for the initial period of exposure to cold (see p. 279), then falls back towards the baseline, although a different level of function of cells is maintained.

Cold increases the acinar cell size, the uptake of iodine and the rate of dehydration of thyroxin by sheep tissues (Freinkel and Lewis[1462]) and rats show a similar pattern. Temperatures above 25° C depress these functions in experimental animals (Dempsey and Astwood[1452]).

For man there are no definitive answers (see p. 269), although Osiba[1536] finds seasonal thyroid changes. Radioiodine studies have been inconclusive so far. On the other hand, Roberts[1546] has drawn together the measurements on basal metabolic rate (B.M.R.) made in different races living in different latitudes throughout the world. There are some difficulties in interpreting the B.M.R. Standardization on American body types does not apply to the smaller and leaner peoples living in the tropics (Galvão[1466], Roberts[1547]). Methods of measurement have differed in both time and place. The control of ambient air temperature has been deficient in some measurements. In spite of all this, it does appear that for a given race living near the pole, the metabolic rate is higher than for the same race living near the equator. Galvão supports this conclusion for Brazilians. In the case of the North American Indian, the metabolic rates for Eskimos and Canadian Indians are higher than those of Brazilian or Mesoamerican types. Interestingly, these

Amerind peoples have higher metabolic rates than Europeans and higher still than Mongolians. On the other side of the Pacific, Mongolian races living in Siberia have higher metabolic rates than those living in the region of Singapore, and the equatorial Mongoloid metabolic rate is lower than that of the equatorial North American Indian. The average findings reported by Roberts[1546] cover hundreds of authors and thousands of subjects. The resting metabolism of hot climate peoples is low and it is unlikely that this difference is merely the result of greater relaxation by tropical people than those living near the pole.

Some aspects of adrenal cortical activity may be reduced in the heat whether in acute experiments or over the hot season. The observation of Robinson, Howard and Macfarlane[1549] that in both the summer period and in hot rooms, urinary excretion of 17-ketosteroids is reduced 25%, has been confirmed by Watanabe and Yoshida[1576] and by Bass' group[1431]. The excretion of 17-ketogenic steroids follows the same pattern (Macfarlane and Robinson[1511]). Hellmann *et al.*[1478] observed this fall in excretion but thought it insignificant. A similar reduction occurs in sheep exposed to a hot environment. Since the eosinophil count appears to fluctuate seasonally (Watanabe *et al.*[1577]) it is possible that there is a seasonal change in the amount of such steroids as cortisol released from the adrenal cortex. Adequate blood studies have not yet been undertaken on the seasonal amounts of cortisol in circulation.

Equatorial climates near sea level present a uniform temperature without clear seasonal change. Equatorial man seems to show little difference from temperate zone inhabitants in body fluid distribution or blood and urine concentration in such regions (for Singapore: Wadsworth[1575] and Whittow[1581]).

Long-term adjustments

(1) *Seasonal responses.* In contrast, human groups living in the subtropics or on a continental area where rather wide summer-winter differences in temperature are encountered, show seasonality of function. The subtropical effects are seen in societies living between 30° and 10° north or south of the equator. In the centre of continents, high summer temperatures are encountered, up to 40° from the equator. Each year as the seasons change, some degree of acclimatization is acquired for heat and for cold. With the spread of air conditioning and control of the environment, these fluctuations will probably grow less. There are, however, sufficient unsophisticated communities still to make seasons measurably the moderators of human function (Fig. 77). In New Orleans, Burch[1436] found evidence that metabolic

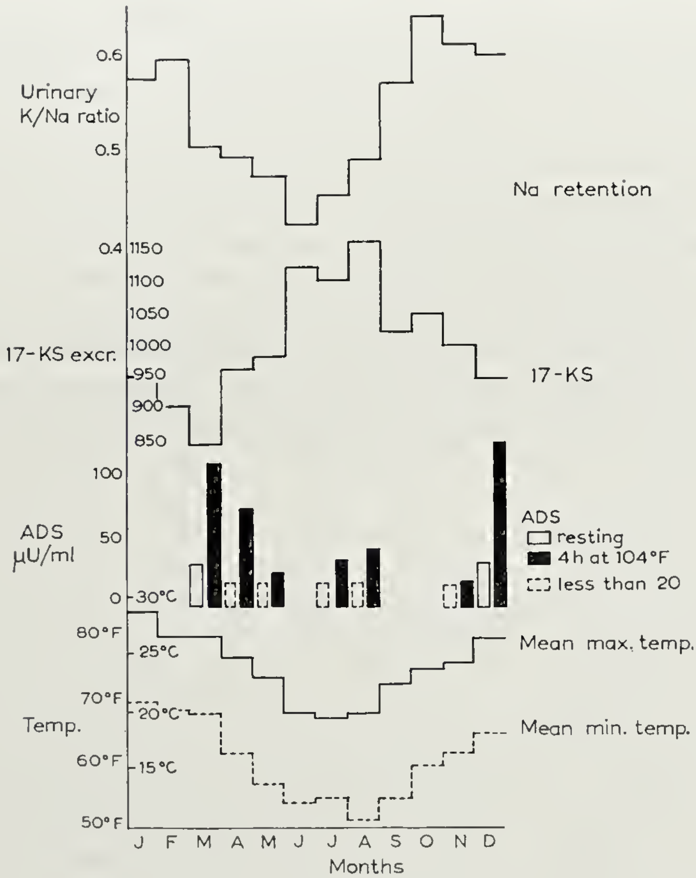


Fig. 77.

Seasonal changes in excretion of sodium and 17-ketosteroids and release of antidiuretic substance (ADS, probably ADH) into the plasma on heating. The data are derived from 7 adult subjects studied on 27° S latitude. During summer there was a high K/Na ratio (probably due to aldosterone activity associated with sweating), and a decreased 17-ketosteroid output. About 2 months after hot weather and sweating began there was an increase of ADH in the plasma both at rest and on heating to 41° C for 4 hours. There is seasonal water, salt and endocrine adjustment, apparently to sweat production (after Macfarlane).

rate was increased by the hot and humid environment presumably because heart work was increased by such a summer climate.

A seasonal change of metabolic rate would be expected in regions where the summer-winter temperature difference is greater than 10° C. In Japan at Kyoto the mean monthly temperature ranges from 8° to 27° C, and Osiba[1536] correlated this with an increase in B.M.R. of 6.6% for each 10 C rise of mean temperature. Similarly he found a winter increase of 60% in the plasma bound iodine level, relative to summer. Other reports on seasonal B.M.R. changes are not so clearly defined.

Other seasonal variations are water turnover, which is high in summer, as is renal conservation of sodium. Sweat electrolytes are reduced in concentration. There is increased plasma volume in the hot season and a ready production of ADH. Less 17-ketosteroid and 17-ketogenic steroid is excreted in the urine, and there is evidence of lower thyroid function during summer (for further details on seasonal influences see p. 575).

(2) *Water metabolism.* The intake of water varies with age and temperature (Fig. 78) as well as with personal tastes and idiosyncrasies. In any environment in which there is sweating, there is increased water consumption. At a neutral air temperature there appears to be a greater basal (non-thermal) sweat rate on the finger in winter than in summer (Mackinnon and Mackinnon[1519]). But thermal sweating is obviously greater in amount in summer than in winter.

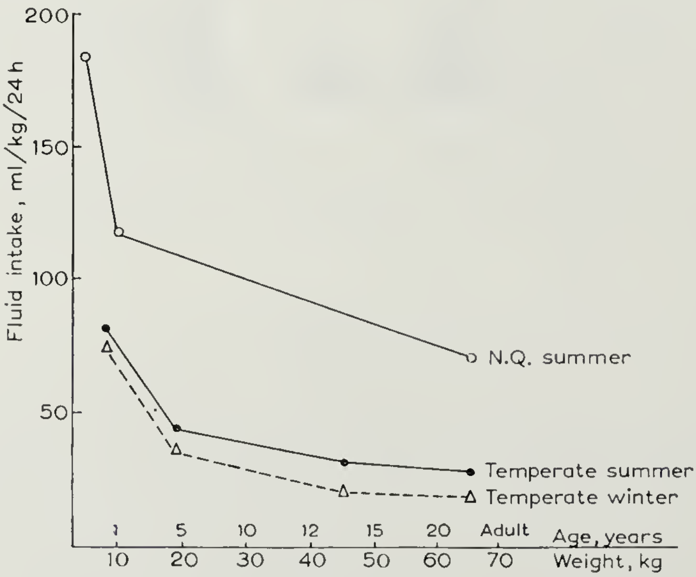


Fig. 78.

Changes of fluid intake with age and ambient temperature. In the tropics there is a higher intake at all ages than in temperate regions, and the intake/kg is greater in infants than in older people. There is a relatively greater water turnover by infants than by adults at any temperature. Estimates from Crosby and Shepherd and unpublished observations, on subjects at rest or performing light work. N.Q. = North Queensland, latitude 23°–11° S (after Macfarlane).

The seasonal pattern of water excretion is the reciprocal of that of water intake (which increases with sweat production) in any subtropical or continental temperate zone. In summer about half the volume of urine is excreted relative to winter. The concentration of urine increases as the volume falls. In winter there is no measurable ADH in the plasma, and it is only towards mid-summer that ADH is induced by heavy sweating to appear in quantity.

The distribution of water in the body follows a seasonal pattern with some increase in summer relative to winter. Plasma volume and interstitial volume are both increased in the hot period.

(3) *Sodium status.* There is a moderately well marked seasonal range of urinary Na/K ratio (Macfarlane[1508]). In the subtropics, Na is less likely to be lost with the urine during summer than during winter (Fig. 77). The difference is represented by the Na lost in the sweat. This Na/K ratio probably corresponds with a seasonal fluctuation in the amount of aldosterone secreted by the adrenal. So far, this seasonal pattern for aldosterone has not been measured. There is, however, good evidence from Australia, Japan and America that the excretion of 17-ketosteroids and 17-ketogenic steroids is increased about 30% in winter above the level found in summer. This pattern is reciprocal to the Na/K ratio and it appears in acute experiments also that aldosterone is increased on occasions in the heat when the ketogenic steroids are decreased, at least in the urine. This is further evidence of the independent regulation of these two types of adrenal steroid.

(4) *Reproduction.* Mills and Senior[1529] pointed out that there was a rate of conception in the cold regions in the United States during summer, different from that found in the more tropical zones. In Florida there was a 30% decrease in expected reproduction in the heat of summer relative to the conception taking place during winter. In the cold regions, optimal conception seemed to occur in summer with a reduction in winter. This pattern has been found also in Australia, where there is a white population extending from 44° to 11° latitude along the coast of the continent (Macfarlane and Spalding[1513]). In the most tropical region, the acclimatized people conceive about 25% less frequently at the height of summer than in winter. Since this pattern is reversed in Tasmania, the length of daylight is not the operative factor. Assuming that temperature has this effect on conception, the endocrine status or behaviour of the population could account for the differences there have been found. It is singularly difficult in a human group to determine the causative mechanisms underlying these population responses. In rats, however, (Macfarlane *et al.*[1515, 1516]) it is possible to induce a general hypopituitarism by rearing the animals in a hot environment, with fewer ovulations on acclimatization. Similarly, sheep and rabbits show reproductive disturbances, with resorption of foetuses during heat.

Short-term responses to ambient temperature

Apart from the day-night changes associated with sleep and waking, there are superimposed thermal changes each day, as sequences of cyclones and anticyclones pass. In cool environments a larger volume of water and salt is excreted during daylight hours than at night. Even with the reversal of sleep rhythm, this pattern of excretion tends to be retained (Rosenbaum *et al.*[1551]). This rhythm is reversed in disease of heart, liver and kidney, however. In a hot environment when sweating occurs mainly by day and is less at night, there is a reduced Na output by day, and more Na and water are excreted overnight. In the sequence of hot and cool periods which occur constantly in any environment, except the most equatorial, there is a flux in water redistribution patterns and day-night ratios change with temperature. Exercise on a hot day reduces 17-ketogenic steroid and also Na excretion (Robinson and Macfarlane[1548]). During a hot period, renal excretion of water, Na and Cl is reduced, but about 24 hours after a cold front has appeared, there is Na diuresis with relief of the tissue turgor which usually occurs in the heat. Endocrine adjustments and circulatory changes underlie these events.

Infants in hot climates

There is little quantitative information on the reactions and fluid turnover of children in the tropics. Temperate zone children, however, have more extracellular water and a greater relative intake of water than adults. When sweating intervenes the turnover of water is increased.

Infants less than 4 months old do not concentrate urine readily, so that they may rapidly become dehydrated if they sweat while water is not sufficiently replaced.

TABLE 33

RATE OF SWEATING OVER 6 HOURS AT REST IN A STANDARD ENVIRONMENT

Number of subjects	*Age*	*Evaporative loss, ml/kg/h*	
		average	*range*
3	9–12 months	6.4	4.2–8.0
3	13–24 months	3.0	2.0–3.7
9	adults	2.3	1.6–2.9

Rate of sweating over 6 hours at rest in a standard environment (35° C dry bulb, 30° C wet bulb). There was more sweat per kg in the infants than in adults.

There are some data from 7 to 24 months old children which indicate that in the heat they (*i*) produce more sweat per kg/h than adults (Table 33); (*ii*) have lower sweat concentrations of Na (1.8–7.6 mequiv./l) and Cl (2.5–11.3 mequiv./l) than adults (30+ mequiv./l); (*iii*) excrete less urine on heating, but more per kg than adults; the urine Na/K is less than 1.0 (Cooke *et al.*[1446]); (*iv*) retain water in the extracellular space (Cooke *et al.*[1446]) in association with Cl; (*v*) have a diuresis delayed 24–36 hours after a period of heating; (*vi*) eat less and drink more (Cooke[1445]) than when cool.

Cooke *et al.* studied three boys in Hartford, Conn., between the ages of 7 and 16 months. The data are limited, as are those shown in Table 33 derived from 6 children acclimatized to the Australian subtropics (unpublished observations). Much more measurement of infants and children is required for firm conclusions. With increasing age, however, fluid intake per kg falls (Fig. 78), in both temperate and tropical populations (Crosby and Shepherd[1450]). But it appears that a 7 kg *child at rest* with the air temperature reaching 44° C in the Australian tropics has a water turnover of 185 ml/kg/24 h (unpublished observation). This may be compared with that of *men working* to their limit cutting cane at 33° C, who consumed an average of 128 ml/kg/24 h (Macfarlane[1509]). The child of 7 kg would then take in and lose 19% of its body weight each day at rest. This equals the greater part of its extracellular fluid: while the cane cutter working hard, turns over 13% of his body weight. Acclimatized infants appear to adjust well to these rates of exchange if given steady water supplements. *Amongst unacclimatized babies, however, a sudden heat wave may produce heat stroke and death.* This occurred in Melbourne (lat. 37° S) in January 1959, when 47 infants (mainly 3 to 10 months old) were known to suffer heat stroke from air temperatures of 41–44° C, and 14 died. The practical implication of these events is the use of dilute feeding mixtures and large water supplements to infants during hot weather (Norman and Pratt[1534]). The other disabilities of children in hot climates are much the same as those of adults (Leithead and Maegraith[1503]).

Limiting environments

There is military and industrial interest in the short and long-term limits of environment in which man might work. It is useful to be able to predict the time of useful performance in aircraft on the ground in the tropics, or travelling at supersonic velocities; the tolerance time of men near furnaces or in engine rooms; or the effects on work of impermeable clothing used to protect against atomic and thermal radiation or chemical contaminants.

Estimates of tolerance have been based mainly on sweat rate, heart rate or heat load.

(1) *Sweat rate.* It is possible to maintain a rate of sweating of about 3 l/h for 2 to 3 hours. Higher rates and longer durations are not possible because water replacement at more than 50 ml/min is not tolerated. In this context, sweat rate is a useful measure of the stress, as in the 4 hour sweat rate index (P4SR) of McArdle *et al.*[1501]. This combines not only the thermal stress, but

also the endogenous heat production from work. The limiting P4SR is 4.5 l (Ladell[1497, p. 66; 1495]).

The heat stress index of Belding and Hatch was found by Turner[1571] to give satisfactory agreement with performance by British workers. The test assumes that continuous work is too uncomfortable when the sweat rate rises above 1 l/h (which is given the value of 100). Lower sweat rates are expressed as percentages of this value.

(2) *Heat load*. The increment in heat storage (kcal/m²/h) may be estimated from weighting the rectal temperature rise as 0.67 and the mean skin temperature rise as 0.33 and assuming the specific heat of the body to be 0.83 kcal/kg/°C. Craig *et al.*[1447] used this approach to the determination of voluntary tolerance by men wearing protective clothing. They found that a storage of 400 kcal/m²/h was tolerated for only 10 minutes, whilst a net gain of 50 kcal/m²/h was endured for 1 hour.

(3) *Heart rate*. Since the circulation is vulnerable when there is physiological strain, heart rate is a useful indicator of environmental limits. Craig *et al.*[1447] estimate that if a heart rate of 160/min is reached in 1 hour, the environment will be tolerated for about 1.3 hours. There is a linear relationship between heart rate and tolerance time. Wyndham *et al.*[1586] recommend relief from work when the pulse rate reaches 130/min and the rectal temperature 39° C.

A stress-strain diagram has been produced by Lee[1501] to describe the known limits of human work. A modified form of this is presented in Fig. 79.

At rest, as Blagden showed in the 18th century, it is possible to tolerate temperatures of about 120° C for half an hour without serious disturbance. The skin becomes dry and rather scorched in such circumstances, but as long as sweating persists, it is possible to keep the body temperature down for a short time.

In practice, light work is commonly carried on at temperatures of 50° C dry bulb in desert areas. The consumption of 8 to 12 l of water per day is necessary for survival in these circumstances (Hunt[1482]). With humidities below 30% most people can remain in good health and in reasonably efficient states at 50° C for 3–4 hours each day.

In humid climates, the limit is considerably lower (see p. 224). With relative humidity above 65%, it is difficult to obtain proficient performance at temperatures above about 33° C, even when air movement is high. Cane-cutters, for instance, at such a temperature consume 9 l of fluid a day and manage to cut 50 tons of cane a week during three hot months (Macfarlane[1509]). Mackworth[1520] showed, however, that in a combination of muscular effort (which increases the endogenous heat) with skill, as in laying a heavy gun, there was a falling off in efficiency at temperatures above 32° C. Good telegraphists at 41° C made 100 mistakes per hour, compared with 8 per hour at 29° C (Ellis[1457]).

At the industrial level, surveys have been made in the United States, Britain and India recently to compare the output and tolerance limits for these groups. There seems to be very little difference (Fig. 79) between the acclimatized cotton workers of India and American subjects, in their upper limits of tolerance and in their performance in the saturated air of cotton mills (Mankiker[1527]).

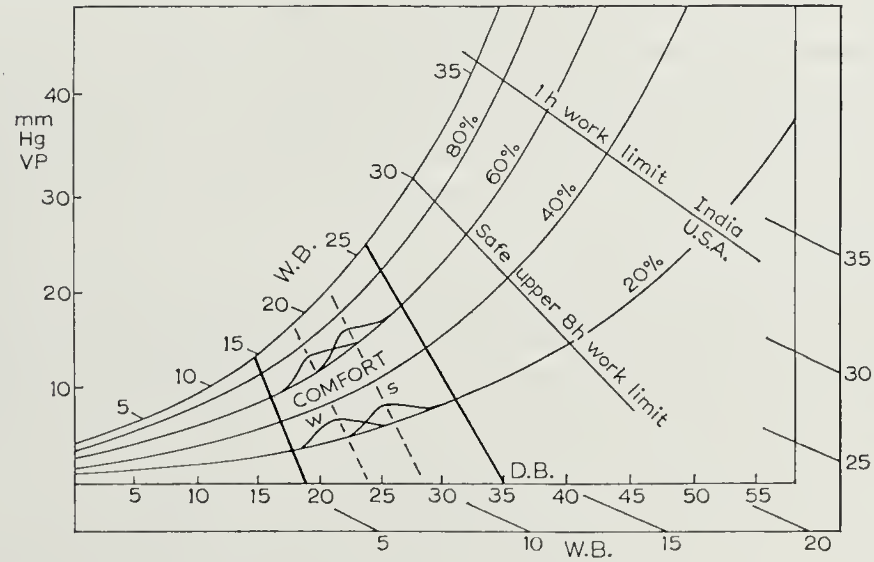


Fig. 79.

Comfortable and limiting environments. The relation between wet and dry bulb temperatures (but not radiation) are represented on a psychrometric chart (after Lee [1500]). The distribution of judgements of comfort for winter (w) or temperate zones, and summer (s) or tropical regions (Table 31) is represented by normal curves drawn on the humidity lines. The modal values of comfort are indicated by dotted lines (....) and the range by solid lines (—). The safe upper limit of factory work for 8 hours is shown (....) at a wet bulb temperature of 30° C (Mankiker[1527], from the work of Ashe). Wyndham *et al.*[1586] put the work limit for Africans a little higher. The rate of working and the air movement obviously influence the limiting zone, however. Work for one hour is likely to produce collapse in conditions found along the upper line, from 36° C at saturation (—) (after Macfarlane).

2. *Dysfunction in Hot Climates*

Introduction

Expectation of life has been and to some extent remains shorter in equatorial regions than in temperate zones. Parasites and their vectors, together with lack of industrial wealth and urban organization, have been the main mortal factors.

Several conditions (such as prickly heat, otitis externa and renal calculus formation) occur commonly during the stages of acute exposure and early acclimatization. This was observed during the military operations in New Guinea (Knott[1489]). Amongst long-term residents in these tropics, there is not a high incidence of calculus. Knott reports only 32 cases amongst 7000 other conditions in his experience of an acclimatized community at latitude 17° S. In Israel, also, newcomers suffer a high rate of calculus formation, but adapted residents have less of the condition (Toor[1570]).

Heat, humidity, aridity and radiation as such can, however, disturb human function and produce illness. *Three main consequences of a hot environment may lead to disability and ultimately to death*: (*i*) Failure of cooling (through sweat gland or water deficiency); (*ii*) Failure to adjust the electrolyte status, particularly that of sodium; (*iii*) Loss of water sufficient to reduce the blood volume and circulatory efficiency. There are variations on these primary themes, but they represent the main causes of disabilities in the tropics.

The classification and naming of these disease processes has been a mixture of folk lore, medical tradition and intrusions of analytical method. A Committee of the Medical Research Council of Britain (Weiner and Horne[1579]) has codified heat disorders, essentially on an aetiological basis, and correlated them with the International Statistical Classification (Table 34). This code is

TABLE 34

CLASSIFICATION OF HEAT DISORDERS ON AN AETIOLOGICAL BASIS

Radiation	(a) short wave: sunburn and skin cancer (b) long wave: heat syncope and conditions listed below
Air temperature and humidity	(a) circulatory disturbances: oedema, static fainting (b) exercise exhaustion
Consequences of sweating	(a) water loss: dehydration, exhaustion (b) salt loss: heat cramps, exhaustion (c) salt and water deficit: circulatory failure
Sweat gland disorders	(a) incomplete occlusion and inflammation of ducts: prickly heat (b) occlusion of ducts: anhidrotic asthenia (c) failure of evaporative cooling: hyperthermia, heat stroke
Affective disorders	heat fatigue states: acclimatization reactions, chronic tropical fatigue
Skin diseases	bacterial and fungal

designed to clarify both the practical handling and the statistical accounting of heat illness. For the present purpose, however, these conditions may be grouped according to the main apparent causes. There is often overlapping of several factors, but it is useful to consider these illnesses as failures to adjust to the environment in one major respect, in the presence of other and subsidiary disturbances.

Effects of solar radiation

(1) *Radiation* from the sun produces sunburn by the action of the longer ultraviolet wavelengths centred round 2970 Å. These penetrate about 1 mm into the epidermis and produce a photochemical reaction on absorption (See p. 339). The chemical action has a latency inversely proportional to the skin temperature, and appears as inflammatory erythema, with swelling of cells, extracellular oedema and pain (Blum[1434]).

After 2-3 days, increase in pigmentation of skin cells takes place and the melanin darkens under the influence of violet light (4200 Å). At the same time increased thickening of the epidermal horny layers takes place. This appears to be a major component of the resistance to sun which many people acquire on continued exposure.

Negroes can become sunburnt if not accustomed to sunlight, though there is a little protection offered by melanin in corneous cells against penetration of ultraviolet light. Ultraviolet light in the 3000 Å region is partly absorbed by a layer of vaseline, by salicylic acid or its phenyl derivative (10%) and by paraaminobenzoic acid (15%) or other aminophenols. These substances provide some protection against sunburn (Ladell[1497]).

(2) *Skin cancer.* Repeated exposure of light skinned people to sun almost certainly leads to plaques of hyperkeratosis on face and hands. High growth rate of epidermal cells may after 20–50 years lead to epithelioma or rodent ulcer. In both the United States and Australia the incidence of skin cancer is greater the nearer the equator the white population resides. Queensland, lying between 28° S and 11° S latitude has a white population with a skin cancer rate of over 2200/million/year. This is probably the highest cancer rate in the world. In Texas, 2000 cases/million are recorded, compared with 200/million near the Canadian border. Dark skinned races, even Mediterranean types, are much less affected by skin cancer than the more northern European groups. It appears that skin pigment is protective against the carcinogenic action of light (for further details see p. 481).

(3) *Long wave radiation,* in the visible and short infarared regions, supplies an important part of the heat load of outdoor workers (see pp. 345 and 346). Unless insulation by clothing reflects or prevents the absorption of

radiation, a man standing in the sun could receive 700 kcal/m²/h. Because of the sun's angle, the small shadow area of man, as well as reflection of incident light, the gain probably rarely exceeds 130 kcal/h. This is still a severe heat load (three times the B.M.R.) and the sequelae of excess heat follow, as they do from the effects of air temperature.

Effects of air temperature and humidity

Exposure of unacclimatized subjects to shade temperatures above 27° C leads to circulatory disturbances.

(1) *Oedema* of the feet and lower leg are commonly found, especially in those standing or sitting for long periods (Zacopoulos[1589]). This becomes less with acclimatization. The oedema is felt most in the hands, which are turgid and it is difficult to flex the fingers to form a fist. The general water retention shows most in dependent parts, and it is temporarily reduced by raising the hands or feet above the heart level. This encourages diuresis.

(2) *Syncope* from pooling of blood in the veins of the legs is not uncommon in those standing for long periods in cool climates. In hot places the effect is exaggerated by venous relaxation (Wood and Bass[1584]). It is interesting in this context, that removal of 400–500 ml blood (for transfusion purposes) is followed by occasional fainting, but the syncope rate increases sharply at temperatures above 25° C. In this type of syncope there is insufficient venous return to the heart, a poor cardiac output and a fall of blood pressure which is sufficient to produce unconsciousness.

Influence of exercise

Exercise in hot regions is a strain that reduces performance. In the Australian tropics, 3 mile races are not held in athletic meetings, because of the difficulty of removing endogenous heat during 15 minutes maximum effort. The rates of running 3 miles in temperatures of 28° C or more are reduced about 30% below those achieved in cool climates. Performance is better when salt and water are adequately supplied (Ladell[1496]).

Exercise in hot, humid environments raises rectal temperatures (to about 39° C in the Burma jungle during the last war) and some subjects become exhausted. It is possible to become accustomed to the sweating and high body temperature, but not all succeed. Recovery from exercise in high air temperatures if often painful, and associated with syncope or exhaustion, as well as with increased 17-ketogenic steroid excretion (Kronfeld *et al.*[1490]).

Consequence of sweating

Relative to plasma, more water than salt is lost in sweat so that dehydration is a primary hazard of long exposure to heat without water replacement. Each year, in the central hot region of Australia, men die within a day because they leave an immobilised motor vehicle to walk in the sun for help. With air temperatures of 40° C and heavy insolation, they sweat perhaps 1.5–2.0 l/h and if without water, they collapse from circulatory failure and die. A rapid loss of 6–8 l of fluid by sweat (15% of body weight) seems sufficient sometimes to destroy a human being exposed to sun without water. Slow dehydration, however, of a Buddhist bishop over 8 days was not fatal, although 23% of body weight was lost (Widdowson[1582]).

The loss of 2–3 l of water from the extracellular space in sweating is partly replaced by intracellular fluid. As the water loss increases, however, plasma volume falls and circulation becomes more inadequate. Tissues lose water, the skin becomes dry and cracked, salivary secretions small and thick, and urine output falls below 200 ml/day. The plasma becomes concentrated, and there are mental disturbances of a hallucinatory or delirious type. Too rapid fluid replacement may cause vomiting (King[1488]).

The wartime studies of men at sea on rafts without water have been summarized by Ladell[1492]. During the first 24 hours, water intake does not aid survival since it largely appears in the urine. On the second day, urine flow falls to 500 ml or less. A carbohydrate diet requires less water for the excretion of nitrogen and phosphorus, than a protein diet. Fat, of course, yields more metabolic water than other foods. Some assistance is claimed from taking about 400 ml of sea water (3-4% salt) since excretion of the salts on a salt-free ration does not require all the water if the urine approaches the human maximum concentrating power of 1400 mosmols/l. On the other hand, mortality on rafts when sea water was taken reached 39%, compared with 3% when it was ignored (Widdowson[1582], McCance *et al.*[1507]). The chain of cause and effect is not complete in this argument, however.

When urine flow is reduced to 300 ml/day or less there is a rise of blood urea and concentration of plasma proteins. There is less rise of sodium concentration.

Tissues are fairly equally reduced in water content, and as this occurs, there is weakness, lassitude and both physical and mental inability to work effectively after 10% of body weight has been lost. When between 15% and 20% of weight is lost there is usually a circulatory collapse (Adolph[1419]). This may be contrasted with the Merino sheep which survives 31% of weight loss by dehydration over 6–10 days (Macfarlane *et al.*[1514]).

In hot climates, sweating even at rest can produce a 10% water loss in two days. Shade and substitution of sweat by evaporating sea water from clothing are important, therefore, in survival in lifeboats. On land it is wise to seek shade by day and travel by night, if there is no water.

Sweat gland disorders

(1) *Hyperthermia.* Periodically in regions where high temperatures are not commonly experienced, a heat wave produces death from hyperthermia. These periods of high temperature (38° to 40° C dry bulb; 30° wet bulb) afflict two main groups of the population. One is the infant in its first year, and the other, those over 50. In the older age group, there usually is some concomitant disturbance, such as alcoholism, arteriosclerosis or metabolic disease. In the infants, no obvious predisposing features have been observed (except the factor mentioned on p. 229). In all, the essential failure is that of the sweat glands to provide sufficient evaporative cooling. After a period of sweating, sweat gland fatigue or failure ensues, and the deep body temperature rises above the critical level of 107° F (42° C). During a period of heat exposure the rate of sweating rises for the first 1–2 hours, then falls. The lowered sweat rate seems to be largely a result of gland failure, since the response to direct cholinergic stimulation is reduced (Thaysen and Schwartz[1568]), but central dysfunction is also probable. Leithead *et al.*[1503] give an excellent picture of the syndromes found amongst unacclimatized sailors, in the region of Arabia.

The relatively great water turnover of infants is important in this context. It is not known to what extent infants acclimatize to heat, but they probably do so readily. In those suddenly exposed, however, to a heat wave without acclimatization, there may be loss of sweat at a high rate without adequate replacement. It is strange that more heat deaths in infants do not take place in the tropics. Apparently, however, their acclimatization rapidly assures them of an adequate water intake and the sweat rate is maintained sufficiently for cooling.

Dyshidrosis has been produced by erythema doses of ultraviolet light (Thomson[1569]). For about a week after sunburn he found a 30-40% reduction in sweating. Vesicles formed from blockage of sweat glands, but there seemed also to be reduction in sweat formation. This could lead to reduced cooling.

(2) *Heat stroke.* A more severe grade of hyperthermia, with rectal temperatures of 42° to 43° C presents the same picture, except that consciousness is lost and the possibility of reversal of the heat balance is less. A period of 10 days during which air temperature rose to 45° C with 60% humidity, precipitated heat stroke in Perth amongst older and not well acclimatized residents (Pearson[1538]).

Heat stroke may be encountered during anaesthesia in a hot region, or as a concomitant of malaria. A very similar condition is induced by surgical interference with the anterior hypothalamic region.

Until sweating is restored artificial evaporative cooling must be provided by *sprinkling the skin with water and using a fan,* until the rectal temperature is lowered to 39° C.

(3) *Effects of salt deficiency.* Reduction in the sodium status of the body leads to two main disturbances: (*i*) Poor physical performance and lassitude, and (*ii*) Heat cramps. There may also be a water and sodium deficiency syndrome in which there is little thirst, but failure of the circulation takes place. In the acclimatized human, there is, if salt intake is low, a considerable sparing of Na excretion in both sweat and urine. It is possible to maintain a sweat rate of 10 l/day on less than 20 g/day of salt intake if the sweat contains 1.5 g of NaCl/l. as it does in tropical subjects. In unacclimatized people (and in some who cannot form dilute sweat) the depletion of salt which may occur on heavy sweating in a heat wave or during work near furnaces, is accompanied by heat cramps. During the period of salt and water loss, little trouble is experienced.

Surgeon Commander Fairley R.N. described *heat cramps* in stokers who had taken too much water during hard steaming in a hot climate (Moss[1531]). "The abdominal muscles and those of the arms, legs and thighs may together or in turn become bunched up with hard knots standing out on the muscle due to violent tonic local contraction. The condition is obviously extremely painful, the man writhing and yelling out during the more acute spasms". It was observed by Moss[1531] that some miners working in hot pits were susceptible to cramps, whereas others of the same acclimatization, working in the same place, were not. He collected evidence that salt was deficient in men prone to cramps. With A. V. Hill and J. B. S. Haldane, he examined a miner from a 38° C shaft, who suffered from cramps. They found that his urine "gave not even the slightest cloudiness with silver nitrate". This they attributed to shortage of chlorides in the blood, which could not be the result of sweating alone. Rather it was the combination of excessive sweating and drinking of water that produced water poisoning and cramps. They found that drinking 0.25% sodium chloride made the cramp-prone men feel better at the end of a day's work, and prevented the muscles from spasm. In those who did not suffer cramps, salt had little effect and some men were nauseated by it. McCance[1505] observed quite large differences between individuals in their liability to salt depletion on a low salt diet. Clearly in the cramp syndrome, individual renal, endocrine and metabolic factors are active, as well as the hot environment and excessive water replacement.

Ladell[1493] had the opportuinity to study heat cramp both in the Iraq desert and in the laboratory at Queen Square, London. The knotting of the muscle in cramps was preceded by fasciculation, as successive muscle bundles went into contraction. This occurred when plasma chloride was reduced to about 80 mequiv./l (though others had found cramps at 100 and 60 mequiv./l). There were no changes in the electroencephalographic patterns, but the electromyograph showed intermittent action potentials. Relief of the cramps followed injection of sodium chloride (23 g) by vein, and if a tourniquet was on a limb before the injection, no cessation of cramps occurred until the circulation was restored and sodium reached the muscle. This supports the concept of salt deficiency as an important factor in cramp production, but water surfeit seems also to be involved by producing a relative water intoxication.

The syndrome is likely to occur in susceptible people when (*i*) over 20 g of salt is lost by sweating; (*ii*) intracellular hydration occurs with dilution of the extracellular fluid by water ingestion; (*iii*) the subjects are unacclimatized and lose more salt in sweat or urine; or when subjects are fatigued.

From the military point of view, the need to supplement troops with salt has been widely discussed. It is clear (Malhotra[1525]) that acclimatized soldiers are quite as efficient on 15 g a day as they are on 25 g day of sodium chloride intake. Acclimatization processes, however, may not be efficient and it is probable that the supply of 10 g a day of extra salt to troops or colonists in the first month of exposure in the tropics may help them over this adjustment period.

(4) *Prickly heat* (*Miliaria Rubra*). In persistently hot and humid regions prickly heat develops usually within 6 months of exposure. Sometimes the condition shows earlier but most subjects are well acclimatized (Sulzberger and Emik[1564]). There seemed to be no predisposing features in the U.S. army experience on Guam. No familial, sex, colour, age or occupational incidence was detected. On the other hand residents within the tropics over many years seem not to be prone to the condition (though susceptible persons presumably leave for cooler climates).

Indian and Negro children as well as adults may be affected.

The skin of the trunk, and to some degree that of the limbs, develops red papules which prickle, burn or itch. Discomfort is increased by exercise and sweating. Essentially the lesion (described first in 1893) is a blockage of eccrine sweat gland orifices by squamous cells (Sulzberger and Zimmerman[1565]). On sweating, some glands produce vesicles in the epidermis and thus raise clear papules with pressures presumably up to 250 mm Hg. Partly blocked ducts are surrounded by mild inflammation. The face sweats freely as do unaffected parts of the body, but prickly heat areas yield little sweat to the surface.

A period of cool weather relieves the symptoms, though anhidrosis may persist for several weeks in a temperate climate. It is difficult to clear the hyperkeratotic plugs from the duct openings by salicylates or other desquamating substances. The only satisfactory relief comes from a return to air conditioned or cool quarters.

(5) *Tropical anhidrotic asthenia* (*Miliaria Profunda*). In 1944 Allen and O'Brien[1422] suggested that one aftermath of prickly heat was anhidrosis which resulted in poor performance in hot zones. The patients were soldiers in tropical Australia and New Guinea, with large areas of plugged pores which became vesicular when sweat was secreted. The skin remained dry except on the face. Evaporative cooling is inefficient in this condition so that some hyperventilation may occur, and the body temperature rises on exercise to 39° C. Anxiety, weakness, poor exercise tolerance and heat exhaustion result from the inadequate cooling (Sulzberger *et al.*[1566]).

Relief is obtained by return for some weeks to a cool environment. Sweat may be released by desquamation, which frees the ducts. Erythema doses of ultraviolet light can be used for this purpose.

Affective disorders

When heat is gained from the environment, there is less drive to engender more heat by activity. This lassitude is commonly found in hot regions and is probably physiological, but it is exaggerated amongst those who have emotional difficulties.

Critchley[1449] has discussed psychotic reactions which seem to be commoner in hot regions—manic outbursts such as amok. Quantitatively, however, the neurotic syndromes are more important and may be grouped as tropical fatigue (Macpherson[1521]). Probably many factors lie behind such states. Displacement from normal surroundings and activity, discomfort, reduced food intake and increased alcohol consumption, parasites, skin rashes and lack of diversion may all contribute. It is likely, also, that some people are unable to make the physiological adjustments needed to live efficiently in the tropics. Full adaptation to hot climates seems to require a new generation. Some part of the neurotic, neurasthenic or tropical fatigue syndrome may be due to inadequate water, salt and metabolic adjustment as well as the emotional disturbance (Lee and Macpherson[1502]).

Skin disease (see p. 563)

In hot environments there is a high incidence of skin infection by pyogenic bacteria and fungi. Parnell[1537] records a dry season skin disease rate of 6.2/10,000/day for fungal and pyogenic lesions compared with 15 during the cooler but very humid monsoon period in India. Repair was slow during the wet months. A similar high incidence of skin infection has been reported in

New Guinea (Macpherson[1521]) and it is clear that it presents one of the major causes of disability in the tropics. Men in warships in the tropics suffer more skin disease and accidents than those in cooler regions (Ellis[1457]). A collection of statistics from the British Navy (Smith[1557]) confirmed this, and showed that the sickness rate trebled as the temperature rose from 15° to 32° C (see p. 245). The main increase in morbidity was from skin lesions, which rose steeply as soon as sweating became common, at temperatures above 27° C. Morale is hard to maintain where there is discomfort and disfigurement of the skin.

Tropical ulcers occur on both acclimatized and non-acclimatized persons, mainly around the ankle. There appears to be a relation between malnutrition, low economic status and the incidence of these slow healing ulcers. Infection with *Borrelia vincentii* is commonly found, and the ulcers are offensive to smell. They are painful and spread rapidly (O'Brien[1535]).

Rest, vitamin supplements, skin grafting and antibiotics assist recovery.

Nutrition in the tropics

All animals, including man, require and take less food in hot than in cool climates. The reduction in appetite is related to positive heat balance. Johnson and Sargent[1483] have plotted the inverse relationship between air temperature and calories ingested. Additional water and more than 5 g/day of salt are necessary for life in air above 27° C.

There are, however, some largely tropical diseases in which proteins and vitamins are concerned. Deficiency of nutrients gives rise to different syndromes in cool and hot regions. At Wupperthal in Germany, undernutrition led to hunger oedema, hyperkeratosis and wasting (McCance[1506]). Scurvy and vitamin A and D deficiency are more commonly found in cold regions than in the tropics. In contrast, the malnutrition in Singapore prison camps (Smith and Woodruff[1558]) was associated with beriberi (thiamin deficiency), burning feet (pantothenic acid deficiency), urogenital syndrome (riboflavine deficiency), pellagroid syndrome (nicotinic acid deficiency) and various neuropathies (Denny-Brown[1453]).

The differences are probably largely due to the sorts of food available in cool and hot climates. There may be some contribution of the climate directly to the manifestations of vitamin deficiency partly by reduction of the total intake. Climate seems to contribute to tropical sprue (Stefanini[1563]), a disease which is based upon low protein, vegetarian diets. Kwashiorkor is commoner in the tropics than elsewhere, and it also has its origin in protein deficiency. It still is not clear to what extent climate is important in these conditions (Kark *et al.*[1484]).

In *cold environments* extra calories and supplements of vitamins C and D are necessary to meet the increased heat loss and lack of sunlight. In *hot regions,* good quality (animal) protein and adequate B group vitamins, together with vitamin A, fluids and salt, are the most critical aspects of diet.

3. Acclimatization to Cold

When the body tends towards a negative heat balance, at air temperatures below 20° C (clothed, at rest) or 28° C (naked), compensatory responses occur. Skin temperature is recorded probably by Krause end organs in the dermis, and these discharge as the temperature falls (see p. 210). Some have optima for falls between 36° and 34° C, others from 22° to 20° C (Hensel and Zotterman[1479]). Skin afferents set up reflex vasoconstriction (Pickering[1539]) of the skin of the toes, feet, hands, nose, and ears roughly in that order. Venous pressure rises, and venous volume decreases (Wood *et al.*[1585]). Acclimatization to cold results in rather less total constriction and more arterio-venous anastomoses remain open to allow the extremities to feel warmer. More heat is wasted than in the unacclimatized: there is a "hunting" oscillation of finger blood flow in the cold (see p. 252), with a period of 10–20 minutes (Aschoff[1424]) as the nervous system compromises between warming tissues against frostbite and preventing excessive heat loss. Acclimatization of man in the arctic during winter outdoors (Le Blanc[1499]) led to 45% increase of oxygen consumption. After 6 weeks it had fallen to 35% and after 14 weeks it was down to 23% above the initial level, in a standard test environment of 9.5° C. In addition the rectal temperature fell more as the duration of cold exposure increased. Whether the small fall of 0.5° C in rectal temperature is sufficient to compensate for the reduced heat input is not clear. Heat flow through the skin decreased less on repeated exposure to cold, in Keatinge and Evans' experiments[1485], while the rise in blood pressure and respiratory gasping diminished. With acclimatization the shell (skin) temperature is reduced less, so the hands are not so numb in the cold (Carlson *et al.*[1442]).

Vasoconstriction increases the *insulation* offered by the thermal shell of the body by a small amount—about 0.8 clo. This is small compared with the rate of heat loss, so that other strain responses are induced. The most important is *increased heat production* (primarily from fats) by one or all of three means: (*i*) Increased muscle action (tone or shivering). Mainly the skin temperature and partly the heat content of the body and blood reaching the hypothalamus determine the onset of shivering, which can be stopped by radiant heating of part of the skin surface (Davis and Mayer[1451]); (*ii*) Non-shivering thermogenesis from increased muscle and liver metabolism with a background of thyroid and adrenal hormone action; (*iii*) Voluntary exercise.

Acclimatization to cold is not much assisted by work, since the effects of cold are offset by adequate heat production. Similarly, too effective insulation prevents the full endocrine, nervous and metabolic aspects of acclimatization from appearing. Some degree of body cooling—hypothermia—encourages acclimatization (Adolph and Richmond[1421]). Scholander and his colleagues[1554] have collected evidence that Europeans can become accustomed to sleeping in the cold, while shivering and producing 50% more heat than in the basal state. Some Australian Aboriginals are able to let the skin temperature fall as they sleep without shivering as much as Europeans, and without increasing oxygen consumption until dawn at 0° C. Much of this response appears to be habituation to low skin temperatures with reduced reflex shivering.

Although muscles provide emergency heat through shivering, other tissues also contribute when acclimatization occurs. You and Sellers[1587] using rats at 1.5° C found enlargement of the liver, while liver slices consumed 15-25% more oxygen and contained 50% more succinoxidase than those of animals kept at 22° C. Such cellular changes are not yet known for man; but it is likely that the quantity of enzymes and coenzymes concerned with release of heat from fats and carbohydrates is increased in liver and probably muscle cells. Héroux and St. Pierre[1481] observed that red muscle capillaries (but not those of white muscle) increased in number on cold acclimatization. This may be important in heat production from muscle.

The endocrine components of cold acclimatization are complex. Initially there is increased output and turnover of thyroxin and adrenal cortical hormones. After 3–4 weeks, in rats, the required amount of these adrenal hormones is diminished (Héroux and Hart[1480]). This is the same pattern as other responses to stress in which the initial endocrine outpouring is not sustained as acclimatization continues. Similarly there is an initial diuresis on exposure to cold, with reduction in extracellular fluid volume. The diuresis involves both salt and water (Fig. 74, p. 392). This diuresis does not persist, however, once the new fluid balance is achieved. There is no direct evidence that this diuresis is due to reduced antidiuretic hormone output. It seems more likely that vasoconstriction increases the relative blood volume, reduces the aldosterone output and allows sodium to be excreted. Increased cortisol production would also encourage the unloading of water.

4. Dysfunction in the Cold

Failure to adjust behaviour, peripheral circulation or metabolism in a cold region leads to inefficiency or illness (McCance *et al.*[1507]). The main dysfunctions involve the extremities, which present the largest surface for heat loss from the underlying core (Burton and Edholm[1439]).

Chilblains

These are mild, superficial areas of tissue damage resulting from poor skin circulation. There is then local itching and swelling. Ears, fingers, lower leg and toes are mainly affected, as a result of cold causing inadequate blood flow through those regions.

Frostbite

This follows prolonged and severe vasoconstriction involving large vessels exposed to dry cold near 0° C. Clotting of blood in damaged blood vessels may prevent return of circulation. The tissues are not necessarily frozen, but they may be destroyed if blood cannot return to the member. If there is freezing of tissues, the intracellular changes associated with ice formation also lead to necrosis. Freezing with supercooling, when no ice forms, is more readily reversible. On warming, there is release of breakdown products which cause vasodilatation, swelling, pain and damage to liver and kidney. There may be gangrene if the circulation has been reduced (Lange *et al*[1498]).

Wet cold syndromes

Syndromes, such as trench and immersion foot, are the result of exposure to temperatures below about 12° C for several days (Ungley *et al.*[1572]). The moisture from cold sweat is sufficient to contribute to this type of injury. Initially there is vasoconstriction with pale, cold feet, and tissue damage from ischaemia takes place. Legs become numb and cease to sweat. Hypoalgesia or anaesthesia persists for weeks after the feet have been warmed. After the phase of vasoconstriction there is vasodilatation. The foot becomes painful, red and swollen, with loss of skin, and nerve injury. Blood vessels become permeable, so that plasma and red cells leak into tissue spaces.

The limb remains swollen and painful with loss of sweating and of some skin sensations for long periods after rewarming (Burton and Edholm[1439]).

Affective disorders

Depressive psychoses are said to be more common in cold regions (Critchley[1449]).

In the process of acclimatization to cold neurosis is encountered. As in the tropics, the colonisation of arctic regions leads to social and psychological strains, which are exaggerated by the physiological difficulties of thermal adjustment. Some individuals make the adjustment more readily than others. For those who adapt poorly, climate and social or personal difficulties combine to produce anxiety neurosis.

Conclusion

When man is transferred from a neutral environment around 24° C to hotter or cooler zones, a sequence of adjustments takes place. Those that can be described from current knowledge involve all physiological "systems", under the general control of nervous and endocrine activity. Some adjustment takes place to daily thermal changes. On exposure to a persistent hot or cold environment there is an initial overswing of the functions during the first 2–3 days, followed by a return towards the initial level of cardiovascular, renal and endocrine activity. What cannot be defined is the cellular basis for acclimatization, though there are some hints of changed concentrations of enzymes and rates of turnover of metabolites. Nor is it clear on what basis the long-term adaptations of tropical or arctic peoples rest. A complex of habituation, suitable behaviour patterns, natural selection and adaptive cellular functions probably exists, for future analysis.

Subsect. D. ACCLIMATIZATION TO HIGH ALTITUDES (HIGH ALTITUDE BIOMETEOROLOGY)

by

A. HURTADO*

Introduction

The tolerance to a low pressure environment, where the partial pressure of oxygen is decreased, is effected through a series of integrated adaptative mechanisms which modify the functional activity of several organs and systems in the body. If such mechanisms attain a high degree of efficiency the condition may be termed *acclimatization.*

There is ample evidence to demonstrate that acclimatization to high altitudes is best investigated in the healthy man born and raised in such environment. The constancy of the anoxic condition and probable hereditary or genetic influences are responsible for a high degree of adaptation in this man and his study provides an adequate comparative basis to understand and rate what happens in the newcomer, through his early period of adapta-

* See also pp. 290–301.

tion, to the low ambient pressure. In addition, the elucidation of the factors responsible for what may be called "natural acclimatization", may lead to better methods of raising the tolerance of people suddenly exposed to anoxia.

Most of the data concerned with the characteristics of the permanent inhabitants of high altitudes have been obtained in the Peruvian Andean region, mainly in Morococha, which is a mining town located at an altitude of 4540 m (14,900 ft), with a mean barometric pressure of 446 mm Hg. The Indian native resident in this place has a mean alveolar oxygen tension of about 50 mm Hg and his arterial oxygen saturation is around 80%. This man, consequently, lives in a constant condition of anoxia or hypoxia. His high degree of acclimatization can be judged from evidence of various nature. Historical data[1614] indicate that this native Indian has been engaged in the hard physical work of mining operation for centuries. His rest periods are often employed in several hours of uninterrupted football (soccer) playing. Monge[1622] has shown that the social characteristics of the Inca organization had aspects related to the climatic and environmental factors. Experimentally there is also proof of the amazing tolerance found in these subjects. Comparative studies of physical activity in residents at sea level and at high altitudes (Morococha) have revealed a *longer performance time* in the latter place and also a *higher efficiency*: *less oxygen consumption and lower pulse rate/kilogrameter of work performed*[617]. Velásquez[663] has recently demonstrated in low pressure chambers a much higher ceiling tolerance in the Morococha natives than in men living at sea level. About half of the natives showed an indefinite useful consciousness time at 30,000 ft., and the mean value of this time was 88 $\pm$ 11 seconds at 40,000 ft.

The adaptative mechanisms found in the native Indian of high altitudes may be grouped under two categories, according to their general objective and significance: (*i*) Those which result in an economy in the drop of the pO_2 gradient from inspired air to capillary and venous blood; (*ii*) Mechanisms which at tissue level favour utilization of the oxygen.

Fig. 80 represents graphically the mean values of oxygen tension determined in samples of tracheal and alveolar air, and of arterial and mixed venous blood, all obtained simultaneously (the last one by means of right heart catheterization) in resting healthy men living in Lima, at sea level, and in native residents of Morococha. The pO_2 in capillary blood was calculated according to the formula:

$$\text{Mean cap. } pO_2 = \text{Venous } pO_2 + \frac{\text{Art. } pO_2 - \text{Ven. } pO_2}{3}$$

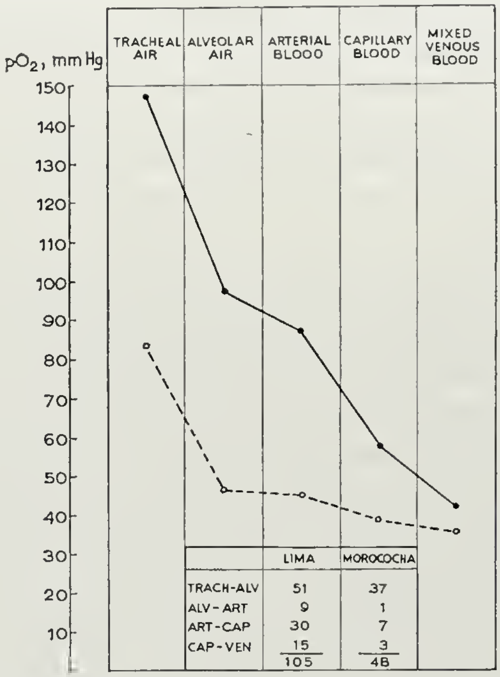


Fig. 80.
Mean pO_2 gradients from tracheal air to mixed venous blood in residents of Lima (sea level) and Morococha (14,900 ft.) (after Hurtado).

It may be observed that the curve corresponding to the pO_2 gradient is considerably flatter at high altitudes. In this place the total drop in the gradient is less than half of what is found at sea level. It means that several adaptative mechanisms operate along the gradient introducing an economy in the progressive descent of the pO_2. Some of these mechanisms may be briefly discussed.

Hyperventilation

It is a well established fact that a man exposed to a low ambient pressure increases his pulmonary ventilation. This process compensates partially the drop in the oxygen tension from inspired to alveolar air and, consequently, allows a higher acquisition of this gas by the circulating blood hemoglobin in the pulmonary vascular bed. It is an important compensatory mechanism. Table 35 shows the mean values of the alveolar gas tensions in resting men in Lima (sea level) and in Morococha (14,900 ft.), and of total and alveolar ventilation. The latter has been calculated with the formula:

$$V_A = \frac{0.864 \cdot V_{O_2} \cdot R}{P_{A_{CO_2}}}$$

where V_A = alveolar ventilation, V_{O_2} = oxygen ventilation, R = respiratory quotient (*i.e.* the ratio of the vol. of CO_2 evolved and the vol. of O_2 absorbed in a given time) and $P_{A_{CO_2}}$ = alveolar carbon dioxide pressure.

The figures obtained reveal that at high altitudes the total pulmonary ventilation and the alveolar ventilation are about 22% and 28% higher than at sea level, and the difference is more signicant if it is referred to body surface area, which is lower in the natives of Morococha.

Experimental observations have shown that the hyperventilation at high altitudes is apparently due to an *increased sensivity of the respiratory center to the* CO_2 *chemical stimulus,* and that this characteristic is not changed by oxygen administration, at least during a short time[1613].

TABLE 35

RESTING PULMONARY VENTILATION

(Subjects in sitting position)

	Lima 103 *subjects*			*Morococha* 80 *subjects*		
	Mean	*± S.E.*	*St. Dev.*	*Mean*	*± S.E.*	*St. Dev.*
Body surface area, m^2	1.71	± 0.01	0.12	1.56	± 0.01	0.10
Alveolar pCO_2, mmHg	39.3	± 0.23	2.4	30.2	± 0.34	3.1
Alveolar pO_2, mmHg	103.9	± 0.38	3.9	50.6	± 0.45	4.0
Total ventilation, l/m (BTPS)	7.77	± 0.12	1.24	9.49	± 0.19	1.77
Total ventilation/m^2, l/m (BTPS)	4.56	± 0.07	0.74	6.19	± 0.12	1.10
Alveolar ventilation, l/m (BTPS)	4.97	± 0.07	0.80	6.39	± 0.13	1.14
Alveolar ventilation/m^2, l/m (BTPS)	2.91	± 0.04	0.43	4.07	± 0.08	0.71

Alveolar-arterial (A-a) pO_2 *gradient*

At sea level, in resting condition, the pO_2 gradient falls about 8–10 mm Hg, when the gas passes from the alveolar air to the circulating blood through the alveolar membrane. Our observations indicate that at high altitudes the drop is practically nil[1614]. This results in an important economy in the pO_2 gradient. This adaptative process is due to a better rate of diffusion, influenced by dilated capillaries and also by enlarged alveoli. Velásquez[1662] has found a definite *increase at high altitudes in the maximal diffusing capacity of the lungs.* The ratio of ventilation to perfusion (V_a/F) is also greater at high altitudes.

Transport of oxygen

The *polycythemia of the high altitude residents* has been repeatedly confirmed. The Morococha native has an elevation in the circulating red blood cells

TABLE 36

CHARACTERISTICS OF CIRCULATING BLOOD

	Lima			*Morococha*		
	number of subjects	*mean ± S.E.*	*st. dev.*	*number of subjects*	*mean ± S.E.*	*st. dev.*
Hemoblobin, g/100 cc	250	15.64 ± 0.05	0.81	83	20.13 ± 0.22	2.00
Hematocrit, red cells, %	250	46.6 ± 0.15	2.4	83	59.5 ± 0.68	6.2
Total blood volume, l	20	4.77 ± 0.12	0.54	20	5.70 ± 0.15	0.65
blood/kg body weight, cc		79.6 ± 1.49	6.5		100.5 ± 2.29	10.0
Total plasma volume, l	20	2.52 ± 0.07	0.29	20	2.23 ± 0.07	0.30
plasma/kg body weight, cc		42.0 ± 0.99	4.3		39.2 ± 0.99	4.3
Total red cell volume, l	20	2.23 ± 0.07	0.29	20	3.39 ± 0.12	0.52
red cell volume/kg body weight, cc		37.2 ± 0.71	3.1		61.1 ± 1.93	8.4
Total hemoglobin, g	20	756 ± 24	105.0	20	1166 ± 38	166
hemoglobin/kg body weight, g		12.6 ± 0.25	1.1		20.7 ± 0.62	2.7

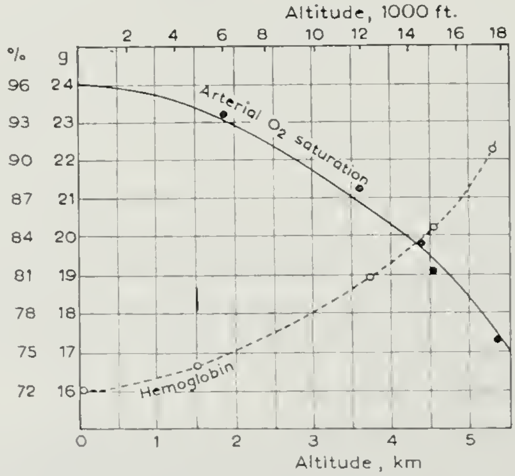


Fig. 81.
Mean hemoglobin concentrations in the blood at various altitudes, and in relation to the mean arterial $HbO_2\%$ (after Hurtado).

and hemoglobin and this is due to an absolute type of polycythemia, with a greater cell volume and a normal or slightly reduced plasma volume (Table 36). The increased cell and hemoglobin content (see Fig. 81) result in a greater transport capacity for oxygen and helps to reduce the fall in pO_2 gradient from arterial to venous blood. It has been demonstrated that the polycythemia is a consequence of a greater erythropoietic activity, as shown by examination of bone marrow biopsies and the degree of utilization of injected radioactive iron[1634, 1637] and it seems possible that the stimulating influence of the hypoxic factor acts through an increase in the erythropoietic factor (erythropoietin) present in the circulating plasma[1620]. The life span of the red cells at high altitudes is normal[1635].

Hemoglobin affinity for oxygen (oxygen dissociation curve)

The main reason for the lesser drop in the pO_2 gradient from the arterial to the venous blood at high altitudes is the shape of the oxygen dissociation curve. At Morococha the oxygen diffusion from blood to tissues takes place in the descending part of the curve, where a change in hemoglobin saturation is accompanied by a small variation in the pO_2. On the other hand, at sea level, where the exchange occurs in the upper flat part of the curve, the lowering of $HbO_2\%$ is associated with a large fall in the corresponding pO_2. There is evidence that the blood haemoglobin of the high altitude native shows a *decreased affinity for oxygen* (Fig. 82) and this favours the unloading of this gas to the tissues[1617].

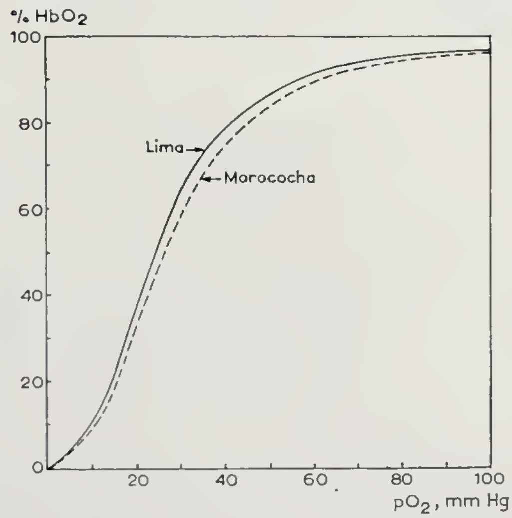


Fig. 82.
Mean oxygen dissociation curves at sea level (Lima) and at high altitudes (Morococha) at standard pH of 7.40 (after Hurtado).

Acid – base balance of the blood

Permanent exposure to a low pressure environment modifies some of the chemical characteristics of the circulating blood. This may be appreciated in Table 37. The lowering of the carbon dioxide tension in the arterial blood,

TABLE 37

GAS TRANSPORT AND ACID - BASE BALANCE IN ARTERIAL BLOOD

	Lima *80 subjects*			*Morococha* *40 subjects*		
	mean	± *S.E.*	*st. dev.*	*mean*	± *S.E.*	*st. dev.*
Blood						
O_2 capacity, mmoles/l	9.30	± 0.06	0.56	12.29	± 0.17	1.10
O_2 content, mmoles/l	9.22	± 0.06	0.56	10.01	± 0.16	1.01
HbO_2, %	97.9	± 0.12	1.1	81.0	± 0.49	3.1
total Hb, mmoles/l	9.30	± 0.06	0.56	12.29	± 0.17	1.10
HbO_2, mmoles/l	9.10	± 0.06	0.56	9.95	± 0.16	1.01
Hb, mmoles/l	0.20	± 0.011	0.10	2.34	± 0.07	0.42
Vc.	0.46	± 0.002	0.02	0.61	± 0.009	0.06
pCO_2, mmHg	40.1	± 0.28	2.5	33.0	± 0.36	2.3
total CO_2, mmoles/l	21.72	± 0.12	1.04	15.87	± 0.14	0.88
H_2CO_3, mmoles/l	1.17	± 0.008	0.07	0.93	± 0.009	0.06
carb.-CO_2, mmoles/l	1.01	± 0.007	0.06	1.73	± 0.032	0.20
$H\,CO_3^-$, mmoles/l	19.54	± 0.11	0.97	13.21	± 0.14	0.87
T_{40}, oxygen, blood, mmoles/l	21.50	± 0.09	0.79	16.83	± 0.12	0.74
T_{40}, at HbO_2 %, mmoles/l	21.57	± 0.09	0.79	17.49	± 0.12	0.76
Buffer base, mmoles/l	49.17	± 0.15	1.31	45.60	± 0.32	2.00
Plasma						
total CO_2, mmoles/l	26.55	± 0.14	1.21	20.73	± 0.23	1.46
H_2CO_3, mmoles/l	1.26	± 0.008	0.07	1.03	± 0.011	0.07
HCO_3^-, mmoles/l	25.29	± 0.13	1.18	19.70	± 0.22	1.38
pH	7.413	± 0.003	0.024	7.390	± 0.005	0.030
Cells						
total CO_2, mmoles/l	16.17	± 0.08	0.74	12.85	± 0.12	0.75
H_2CO_3, mmoles/l	1.06	± 0.007	0.06	0.87	± 0.009	0.06
Carb.-CO_2, mmoles/l	2.19	± 0.009	0.08	2.85	± 0.017	0.11
HCO_3^-, mmoles/l	12.92	± 0.08	0.69	9.13	± 0.10	0.66
pH	7.198	± 0.002	0.014	7.191	± 0.032	0.021

brought about by hyperventilation, is compensated by a proportional decrease of the bicarbonate so the pH is kept within normal limits.

In the electrolyte balance, it has been found that the low bicarbonate is associated with a rise in the chlorides[1616].

Adaptative mechanisms at tissue level

In spite of the compensatory processes which occur along the pO_2 gradient, there is still a decrease in the oxygen tension at capillary level at high altitudes. This requires the presence of adaptative mechanisms to facilitate diffusion and utilization of oxygen in the tissues. There is an important indirect evidence of this occurrence. It has been observed[1617] that *lactate production in the active muscles,* during all degrees of physical activity, is always *lower in the high altitude natives* compared with the sea level residents. This would indicate an adequate oxygen provision or utilization, or both.

One important mechanism seems to be related to an increased capillarity, favouring the physical diffusion of oxygen from blood to the cells. Valdivia[1615] has observed in native guinea pigs at high altitudes, compared with the same animal species at sea level, a definite increase in the ratio: number of capillaries/number of muscle fibers, per mm^2. The increase is about 35%. There are also indications of the existence of significant chemical adaptative processes in the tissues of high altitude native animals. The original observation[1615] of an increase in the myoglobin of acclimatized dogs has been confirmed by later investigations. There has also been demonstrated an increase in the levels of energy-rich phosphates accumulated and in the ATP-ase activity in altitude guinea pigs, compared to those living and investigated at sea level[1660].

Other studies[1658, 1633] apparently point out that the tissular chemical approach to the understanding of acclimatization to high altitudes offers a most promising and important field of investigation.

Pathological aspects of life at high altitudes (Chronic Mountain Sickness)

Constant exposure to a low ambient pressure has a medical interest not only from the point of view of the physiological adjustments which are responsible for the development of acclimatization. The chronic hypoxia may lead to pathological alterations *per se,* or influence the severity of the symptoms of any illness acquired at high altitudes. This field of research has not yet been properly investigated, but the related literature contains already some significant observations (see p. 298). It has been shown[1638] that residents at high altitudes exhibit a moderate degree of pulmonary hypertension, in contrast with a rather low pressure in the peripheral circulation. The factors related to the pathogenesis of this condition are not well understood, but anoxia and an increased blood content in the lungs may play a role. However, the administration of oxygen, at least for a short time, does not modify the elevated pressure in the pulmonary artery.

The most interesting pathological aspect of life at high altitudes is the *loss of acclimatization to the low oxygen tension.* The syndrome, called *Chronic Mountain Sickness* or *Monge's disease,* was first described by Monge[1621] in 1928. It is characterized by an abnormal degree of hypoxia and by an exaggerated level of polycythemia[1611]. The circulating blood volume reaches high values, due entirely to a pronounced elevation of the red cell volume. The plasma volume is decreased. These characteristics may be appreciated in Fig. 83.

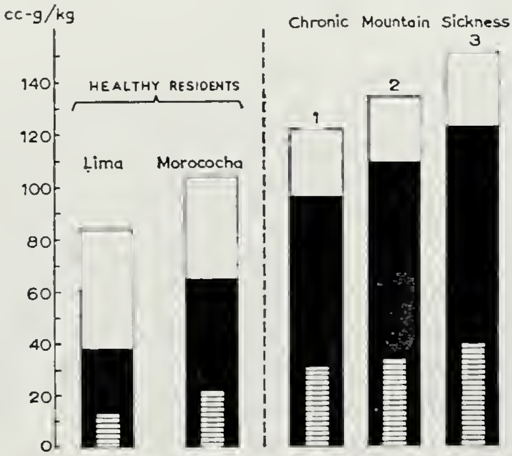


Fig. 83.

Total blood volumes (determined with Evan's Blue) in 3 cases of Chronic Mountain Sickness studied in Morococha (14,900 ft.). For comparative purposes the mean values observed in healthy residents of Lima (at sea level) and in Morococha are also represented (white area: plasma volume; black area: cell volume; crossed area: hemoglobin) (after Hurtado).

The etiology of Chronic Mountain Sickness remained obscure for a prolonged time, but it has been observed recently[1612] that at least some of the cases lack the hyperventilation adaptative process present in the acclimatized subjects, and this leads to a lowering of the partial pressure of oxygen in the alveolar air and a consequent decrease in the arterial oxygen saturation. The abnormal accentuation in the polycythemia appears then to be the possible result of the increased hypoxic stimulus. The respiratory center has in these cases a decreased ventilatory response to the inhalation of CO_2. It is not known whether this alteration is due to functional or chemical changes in the nerve cells, or to circulatory or vascular factors.

Subsect. E. INFLUENCE OF DIFFERENT TYPES OF CLOTHING

by

E. T. RENBOURN

General principles

The environment conditions can be measured by various integrated "temperature" scales and indices (see p. 41) which are based on the short term subjective effects of a few trained subjects exposed (under limited conditions of work and clothing) to different indoor environments, and they have been found of value in assessing thermal comfort in air-conditioned buildings, mines and below decks in ships. Although the somewhat similar "Wet Bulb Globe Thermometer" index has been used, with apparent success, as a measure of the safety for muscular activity in tropical environments, none of these scales and indices strictly apply to the subtle complexities of weather and climate. It is in fact difficult to simulate the solar spectrum, diurnal temperature change or precipitation in a climatic chamber. A hot dry indoor environment can be equated with a warm humid one by means of the *effective temperature* (E.T., p. 41) or *corrected effective temperature* (C.E.T., p. 42) scale, but conditions in a desert area are very different to those of a jungle zone, not only meteorologically but also physiologically, psychologically and biologically[1702].

On a more physiological plane of measurement, the *mean skin temperature* (M.S.T.) has been used as an index of thermal strain, but once generalised sweating occurs as a result of exercise or even rest in a hot environment, the M.S.T. remains constant in spite of a considerable increase in stress. It is, however, of great value in what cases sweat evaporation is insufficient for the demands *e.g.* at extremely high artificial air temperatures (over 200° F), or with heavy exercise when wearing an impermeable garment[1684]. The *predicted four hour sweat rate*[1710] has been put forward as a measure of heat strain on the man under various conditions of rest, work and clothing. However, many individuals oversweat particularly if unacclimatized, and the factor of importance is the sweat evaporated rather than that secreted in a given time. Robinson *et al.* introduced a *heat strain index*[1705] based on the pulse and sweat rate, rectal and M.S.T. It should be remembered that in the tropics the resting body temperature (oral or rectal) of even the indigenous inhabitants is appreciably higher during the hot season[1697].

Skin temperature is a good measure of the subjective effect of cold, but the M.S.T. does not consider the functional importance, in terms of discomfort, pain or frostbite, of small skin areas such as the fingers or toes. The scales mentioned above are not suitable for subzero conditions out-of-doors, and the *wind chill index of Siple*[1709] has not been found of easy application in clothing studies.

Although several human aspects of weather and climate are still in their infancy, sufficient data are available to throw light on the associated problems of clothing.

Elements of textile physiology

The unit of textile clothing materials is the fibre, a variable number of which are twisted together and spun into yarns convertable into the cloth by knitting, weaving or other processes. A characteristic feature of cloth is that it is freely permeable to air movement through the low resistance pathways of its interstices.

Up to recent years textile fabrics have been derived from animal materials —hair (sheep, angora goat, llama, camel, etc.) and the cocoon of the silkworm—and from vegetable fibres such as cotton and flax. Asbestos, the only fibrous mineral, is sometimes used in the manufacture of fire-proof clothing. Animal fibres are protein (keratin) in nature and burn with difficulty compared to the cellulosic vegetable fibres.

Nowadays a great variety of clothing materials are derived from artificial fibres manufactured from either natural or synthetic chemical substances. Artificial fibres derived from natural sources (known by the generic name of *rayons*) are manufactured from proteins (*e.g. Ardil* from peanuts) and from cellulosic materials (viscose and cellulose acetate rayons). The so called synthetic fibres are derived from a number of organic polymers; thus Terylene (Dacron) is a polyester, the various *nylons* are polyamides, and *Acrilan, Dynel, Orlon* and *Verel* are acrylic in nature. Whereas wool, cotton and linen are derived from short or "staple" fibres, silk and the artificial fibres are manufactured as long fairly translucent filaments which lend themselves to the production of thin, tight weaves; but if cut into "staple" lengths (or by the inclusion of loops in the filaments) can be converted into fairly opaque materials with the appearance and feel ("handle") of cotton or wool. Synthetic fibre materials are hard wearing, are more or less shrink-proof and crease-retaining, take up very little water and dry quickly, but many have the disadavantage of melting at fairly low temperatures. It is the *low water uptake* of synthetic fibre materials which is related to their *high content of static electricity,* an annoyance in underclothes but a potential danger in the presence of explosive mixtures especially in a dry atmosphere. On the other hand, it has been claimed by a number of physicians that the static charge may be of physiological value, *e.g.* to those suffering from rheumatism. This assumption, however, is based on no great scientific foundation.

The "warmth" of a cloth is not due to the physical properties of its fibres but mainly to the *insulative still air clinging on to the fibres and yarns* and the relatively still air in its interstices. The wool fibre is covered with surface scales and has a "crimp" or waviness and an elasticity present in few other fibres, natural or artificial. These properties explain the well marked „aero-dynamic drag" of a woollen material, a property which tends to prevent air moving within or passing through it. A great disadvantage of untreated wool is that it shrinks—a property related to the surface scales.

Cellulosic and particularly protein fibres—natural or artificial—take up appreciable quantities of water (vapour or liquid) into their substances, a property which may explain why cotton and wool fabrics can absorb up to about 20% and 40% respectively of their weight without feeling damp to the skin — an obvious advantage in underclothes. Such absorption is associated with the liberation of a large quantity of "sorption" heat. It has been calculated that a wool garment weighing five pounds takes up some three quarters of a pound of water to give out for an hour or more the equivalent of basal metabolic heat. This may in part explain why it has long been believed that wool maintains an equable temperature around the body[1700]. Much has been made of the maxim that "wool is best", but for "sorption" heat to be of value wool must be worn close to the body and over as large an area of skin as possible. This might necessitate a return to the long unpopular woolen "combinations". Preliminary experiments on men wearing three layers of woollen garments showed but little evidence for "sorption" heat effects[1704].

In the presence of rain, wool and cotton can also take up large quantities of water into the interstices. Thus a thick dense woollen overcoat can take up more than double its weight of water. With the air displaced, the thermal insulation of a garment is lost. On the other hand a coarse-haired woollen Harris tweed material wicks badly and can for a short time be fairly shower-proof. Although synthetic materials take up very little water into the fibres, an appreciable quantity may be taken into the interstices by wicking. Nevertheless, under conditions of sweating, synthetic fibre underclothes soon feel unpleasantly damp and are hence not suitable for outdoor sports or for use in a hot climate. The same may but to a less extent be true for varnished "drip dry" cotton materials. In blends with wool or cotton, synthetic fibres retain many of the good properties of both natural and artificial systems. The rain-proofness of "ventile" cotton fabrics is dependent upon the *swelling of the fibres which blocks interstices* but still allows insensible perspiration to pass out. Surface treatment of the yarns by silicones, waxes and certain fatty acids modified surface tension so that water "pearls" into drops rather than spreads into the material.

Rubberized materials and "plastic" films are water-proof (and wind-proof) but impermeable to insensible perspiration which under cool conditions will condense on the inner side. With a backing of cloth this is, however, not of particular disadvantage for short periods of wear. An impermeable layer near the skin will prevent sweat from soaking into the outer clothing. This idea has been used, but not with particular success, in the "vapour barrier" principle for artic clothing[1708]. Natural turbulent winds do not penetrate clothing as easily as do the stream-lined winds[1703] produced in a climatic chamber and out-of-doors during say ski-ing or with exposure in an open vehicle. *Wind-proofness depends upon tightness of weave which closes up the air interstices.* It is clear that for violent exercise and sweating, cotton is much more acceptable for a windcheater than nylon or Terylene, although the last two are eminently suitable for tents, etc. Due to "aerodynamic drag" even open-weave materials cut down low air movement appreciably, a phenomenon well noticed under a mosquito net.

Colour is of no importance in the reflection of the long wave infra-red radiation of low temperature sources such as the earth's surface or the human body, but light colours (*viz.* on a roof, or a white skin) are good reflectors of the sun's short infrared rays (see p. 36). On the other hand, in the sun the differences in warmth between a light and dark coloured suit of the same material may be less than generally believed[1689]. Quite apart from a specific absorptive effect of a dye, textile materials are not continuous surfaces, and heat unreflected from the outer surface of the yarns may be reflected internally to be absorbed by the deeper ones, *i.e.* closer to the body. There may be a similar explanation for the long white hairs and in the short black "guard" hairs of the fur of some arctic animals. The view was held half a century ago that heat stroke (and prickly heat see p. 410) were due to the "violet and ultra-violet actinic rays" of sunshine which could (like X-rays) penetrate ordinary clothing materials but were absorbed by anything of a black or orange colour[1699]. As a consequence, white outer clothing was used to reflect the sun's rays and coloured linings or underclothes worn to absorb the so-called harmful actinic rays. There was no scientific basis to this theory, and it is well known that ordinary clothing (of whatever colour) absorb sufficient ultraviolet light to prevent sunburn. On the assumption that a metallic film (aluminium) reflects the body's long infrared radiation, metallized fabrics (coated yarns with interstices free) have been used for some years as linings in raincoats and light-weight cold-weather clothing, but with little objective success. However, a metallised film (*vis.* aluminium on a very thin continuous Terylene sheet) used as a blanket maintains a higher skin temperature than does the unmetallized sheet[1706]. The sheetings have the disadvantage of being impermeable to water vapour.

The body and clothing

The temperature of exposed or clothed skin varies widely from place to place under conditions of comfort (see p. 230), but it is often stated that the internal body temperature (mouth or rectum) is constant within narrow limits. Variations in temperature (see p. 221) are not to be regarded as impairment of body heat loss ("heat storage") but rather to a variable setting of the body's "thermostat".

Under ordinary conditions of environmental temperature and body activity, three quarters of the heat produced by the body is lost by radiation and convection and one quarter by the evaporation of insensible perspiration (see p. 215). Under conditions of warmth the latter increases as external and skin temperature rise, until at an external temperature of over 80° F generalized sweating occurs and the skin temperature stabilizes (see p. 216). Sweating arising from muscular exertion may occur at any environmental temperature and is a factor of considerable significance in coldweather clothing.

As environmental temperature rises above 80° F, the importance of sweating increases, but in the humid tropics (where the dry-bulb temperature is rarely over 90° F) the extreme humidity impairs evaporation and the skin may be constantly moist. In desert areas humidity is low and evaporation of sweat very rapid. Dry bulb temperatures during the day lie between 90° F and 130° F and, where this is higher than skin temperature, heat is absorbed by convection currents and wind. Radiated heat is also absorbed from the sun and ground. The amount taken up by the nude white body or white clothing (both of which reflect roughly half the incident solar heat) is of the order of 2–4 times the basal heat production[1680, 1681, 1712].

At comfortable environmental conditions (60°–75° F) nudity is associated with a cooler torso and warmer extremities than the clothed body, but the M.S.T. is, however, not greatly changed. A gentle breeze playing on exposed skin reflexly increases muscular tone and may be the background of the feeling of invigoration associated with the uncovered body. Chilling of the skin by wind or wet clothing is said to be associated with the reflex slowing of the circulation of internal organs which is believed to play a part in various diseases.

It may be asked whether without clothing life can exist at low temperatures. The Fuegians and the Australian aborigines sleep nude in the open, with only a small fire as protection, at temperatures down to freezing point.

In spite of being more hairy, men are said to be less resistant to both heat and cold than women[1690] (see p. 231). Most women wear less clothing from top to toe than men under most weather and climatic conditions, but since this is a fairly recent innovation[1686], it is not likely to be due to physiological differences but rather to those dictates of fashion which they so happily accept. Yaglou has carried out some interesting work on this point[1715]. When the fires burn low in old age, more clothing is required for comfort.

Physiological principles of clothing

It has sometimes been said that for civilized man the future of clothing lies in its disappearance[1686]. This need not lead to undue alarm, for even if nudity is accepted on aesthetic, moral and hygienic grounds it is still not compatible with the vagaries of the weather, the severities of climate and the requirements of our daily work or leisurable activities.

One facet of clothing—the textile fabric—has already been considered. A garment, however, is more than the fabric, for it may have a stiffening interlining, extra layers (pockets, etc.) and an inner lining. Laboratory tests of thermal insulation are made on small pieces of unadorned cloth under horizontal conditions. Clothing (except at the shoulders, and buttocks in sitting, etc.) is, however, worn vertically, and the insulating air layers between its constituent garments depend upon their shape, drape and fit to the body beneath. These relatively still air layers can be more important than those within the garments and their fabrics, for at an optimum thickness of roughly a quarter of an inch of air, the insulation may be the equivalent of that of vasoconstricted skin. In this lies the "multi-layer" principle used in arctic clothing[1709].

The design of clothing may itself outweigh the thermal properties of the constituent fabrics. Thus, convection currents from the trunk emerge at the neck opening ("chimney ventilation"), and the movements of walking cause gentle billowing of air under a jacket, skirt or overcoat. The effect of a thin impermeable light-weight "plastic" (p.v.c.) "mac" depends partly upon its design. As a very loose coat it may not produce undue discomfort even during monsoon rain, but in the form of a well fitting suit buttoned up to the neck it would soon lead to profuse sweating and overheating of the body with heavy work in any climate. Clothing worn tightly will decrease the thickness of air layers between the garments beneath and hence *cut down the total thermal insulation.* By restricting movement, tight or bulky clothing (arctic assemblies) will lead to greater heat production for a given amount of exertion. Nevertheless, tight fashionable clothing have been worn in the past by both sexes, and women will no doubt continue to do so in future in spite of all physiological or hygienic considerations[1686].

It is often put forward that leather "breathes". However, compared to a textile fabric, air movement through its substance is negligible and, with the daily polishing of shoes, even water vapour movement must be very small. The virtue of leather in footwear is probably due to the fact that it can *absorb vapour or liquid water from the foot*[1711] (and perhaps liberate "sorption" heat) rather than transmit it to the opposite face. As long as the shoe insole is of absorptive leather, there may be no great disadvantage in the use of an impermeable "composition" outsole for healthy feet[1711]. In any case, if one but considers the frail sandal-like shoes of women, it is clear that the hygiene of their feet is not appreciably affected by the coverings. With entry of water into shoes or boots from without, the seams are (as also in a raincoat) points of particular weakness.

In the presence of cold air, heat loss will be minimized by well fitting (but not tight) clothes, a belt round the waist, a scarf round the neck, by closing other apertures and replacing skirts by trousers. It is difficult to lag narrow pipes because the insulation also adds a greater surface for heat loss. Over the trunk, clothing and air layers of up to a total thickness of about five inches or more will improve thermal insulation, but in the case of the hand gloves thicker than a quarter inch will gradually increase heat loss through the fingers. Tight gloves and boots not only cut down insulation but impede the circulation and may lead to discomfort, chilblains and frost bite. The head occupies but a small part of the total body surface, but since the skin of the cranium and part of the face does not vasoconstrict with cold, the head becomes a *potent source of heat loss.* Even at ordinary temperatures one quarter of the total body heat loss passes through this channel, and at 40° F one half is lost through this "hole in the bucket"[1687]. Wind is kept out by an outer garment of fine weave material (or leather), but the efficiency of a wind-cheater also depends upon its design.

Experiments in a climatic chamber have shown that at temperatures of 90–120° F and under a wide range of humidity, men sweat less in the nude than when wearing tropical clothing. It has also been suggested that when wearing clothing the sweat is much richer in sodium chloride. This has led to the idea that clothing is contraindicated in the humid tropics and may be the cause of *tropical neurasthenia,* probably, in the main, a psychological disturbance[1683, 1702]. However, even under these conditions the demands of convention may still have to be accepted. Suitable clothing prevents sweat dripping off the body, gives an increased surface area for heat loss and when soaked becomes a better heat conductor. In the jungle and water-logged areas, clothing is essential to protect the skin of the body and feet from mud and thorns, fluke and hook-worm larvae, biting and parasitic insects, and from snakes and leeches, etc. Furthermore, there is no real proof that the nude torso is immune to prickly heat[1707] or that salt deficiency[1702] is the cause of "tropical neurasthenia" (see p. 413).

Trials under desert conditions show that men actually sweat more when nude and hence require more drinking water.[1678] The exposed unacclimatized skin will soon become dangerously sunburnt by the high intensity ultra-violet radiation and absorb large quantities of heat. The multiple, loose billowing garments of the desert dweller act as a tent which absorbs heat at a distance from the body and keeps out sand and flies. Such garments are not suitable for work, but they make a good blanket for the desert nights which may be intensely cold. It may be noted that the outer garments of women, and the outer cloak-like garments of the wealthy desert Arabs, are often of a dark colour. The tents of the Bedouin are black (see also p. 37).

Consideration of the clothing worn by both primitive and civilized communities in various parts of the world strongly suggests that the various garments worn developed more out of factors of availability, tradition, social and religious customs than on any considered thought given to protection from weather or climate.

Clothing for weather and climate

A large body of work has shown that, as measured by physiological methods, it is not easy to find differences between garments made of conventional natural fibre materials[1703]. This may be explained, as given above, in terms of the complex dynamic "compensatory" mechanisms which exist not only in the skin but also within and between the clothing layers.

There is no doubt but that at temperatures of about 60–75° F, people vary greatly in the clothing they wear, and most could be acclimatized to wearing less clothing and still remain comfortable. In a temperate climate there is little to choose between the materials, natural or artificial, used for what may be called for simplicity the conventional "three layer" system of clothing worn by men (underclothes, shirt, jacket and trousers) or women. For reasons already given, under conditions of ordinary activity, the addition of a waistcoat or thin pullover may not make much subjective (or objective) physiological difference to most people. The problem of protection from rain has already been considered.

Winter conditions in a temperate climate are sometimes described as "cold damp". There is no evidence, however, that damp air is a better conductor or convector than dry air at the same temperature[1704] (see p. 35). If this is the case, it would appear that the difference between cold damp and cold dry weather (neither of which have been clearly defined) are due to other meteorological factors[1704] (see p. 224). People who near freezing point are habituated to dry "hot houses" in the winter (temperature about 75-80° F) and use warmed vehicles, are prepared to wear lighter clothing both indoors and outdoors than those living in cold houses. They do not complain of the cold because they are not often or for long exposed to it[1704, 1715].

The expression dry cold is sometimes applied to subzero conditions with snow underfoot[1704]. This produces no great problem for the town dweller living under comfortably warm conditions. However, for the arctic explorer the problem becomes greatly accentuated by "wind chill", and by the fact that clothes warm enough at rest become too warm with exertion. The physiological effects of solar radiation are not to be forgotten[1680, 1681]. Sweat passing into clothing destroys thermal insulation and may lead to severe chilling when exercise is stopped. A "frost line"[1708] may form in the outer clothing layers. Clothing should be "opened up" as a drill before sweating occurs, but in the presence of wind this is no easy matter. Since the toes are enclosed together with the rest of the foot in a box-like compartment keeping them warm is much easier than in the case of the gloved fingers. The warmth of a mukluk lies in the insole and socks rater than in the boot "shell"[1711]. Covering the head by suitable hoods is imperative for those in the open for any great length of time. The skin and fur clothing of the eskimo is functionally very suited to the environment, but now that fur and pile fabrics are being successfully made from synthetic fibres, he is showing a preference for the clothes of civilization. In the privacy of the igloo he is a nudist. For further details of the problems associated with arctic clothing, the reader is referred to the excellent work of Siple[1708]. Glare is marked under snow conditions, but "snow blindness" is a variety of photophthalmia[1685] due to the high reflectivity of snow and ice for ultra-violet light[1692]. Goggles with suitable absorptive lenses of a neutral tint (orange may be more "cheerful" for overcast days[1696]) are a necessary prophylaxis.

Under tropical conditions, a skin constantly covered with sweat is liable to prickly heat and fungus infection[1702] (see p. 412), hence absorptive and permeable clothing and personal hygiene[1702] are particularly important in warm damp areas. Although the minimum clothing compatible with conventions should be worn in the latter, the protection requirements of the jungle area itself must be remembered. Garments should be loose, without constricting belts, and ventilation openings (neck, underarm, sleeves, shorts, etc.) cut on really generous lines. Women's clothing easily lend themselves for use in the heat of the tropics, but skin protection may still be required. A thin, fine weave, cotton poplin keeps out biting insects and is not objectively warmer than a thicker but open weave "aertex" material. The bush-jacket has the virtue of combining the shirt with a coat. Starching adds to its appearance and to "chimney ventilation", but on the other hand blocks air interstices. Synthetic fibre materials are at present contraindicated for use in underwear and shirts in any tropical area, but as blends with fine wool, cotton or linen make suitable light-weight suitings. A flannel binder[1700] is still advised by some tropical practitioners to combat the so called "chilled abdomen" which is believed (on insufficient evidence) to predispose to diarrhoea and a "tender belly". It will, like any other well fitting garment, nevertheless produce in most individuals "a nice band of prickly heat".

For reasons given, clothing is an essential requirement in desert areas, but no longer is it believed that heat disorders arise from the sun's rays penetrating the spine or cranium. As a consequence, the spine pad[1699] is almost a museum piece and the "solah topee" (even with a coloured or aluminium lining[1688, 1691, 1699]) worn only for ceremonial occasions. Any light-weight hat or peaked cap is quite suitable. The reflectivity of sand and stone for visible and ultraviolet light is not as high as that of snow[1692, 1696] and apart from irritation from dust, photophthalmia is not an important problem in the desert[1696]. Many people, however, find comfort in tinted lenses[1696, 1702], but to wear them out of the sun is in the main an affectation. A good insulative sole protects from the hot ground, and the addition of a removeable ventilating insole makes for a cooler desert (or jungle) boot[1711]. Sandals should be worn whenever possible in all tropical areas as prophylaxis against tinea pedis. Additional clothing will be required for the cool or cold nights.

Section 4. Influence of Geographically Determined Differences in Climate on Racial Characteristics of Man (Ethnological Biometeorology)

The various aspects of this fascinating subject will be very briefly discussed in this section. The reader is strongly recommended to study refs.[1716 1805] which give a fairly comprehensive review of the complex nature of this important problem.

The geologist and paleontologist, daily faced with the problem of evolution during the last thousand million years, knows from his own studies of stratigraphic sections in the field that a gradual change in the structure and physiological mechanisms of living organisms must have taken place during the history of the earth, changes which are mainly ascribed to a complicated process briefly indicated as *biological adaptation*. The actual mechanism of this adaptation is unknown, although in paleontological literature many theories have been advanced to explain this phenomenon of evolution.

1. Environmental Factors Affecting the Living Organism

The environmental factors which seem to have affected the changes in both the outer appearance and inner structure of the living organisms, can be classified into at least 4 groups.

Changes in food conditions

Owing to movements of the earth's crust and the changes in distribution of the land and sea areas in the world, the chemical composition of the soil (and its trace element content), the drainage of the soil and the type of vegetation have changed.

The composition of the soil changed partly as a result of newly formed rocks on or near the earth's surface (volcanic activity, sedimentation, etc.), partly on account of soil weathering (the complex interaction between the weather and climate of a region and the soil), which is affected by altitude, topography, drainage, geographical latitude and so forth.

Changes in composition of the soil, of the drainage (depending on topography, composition and structure of the soil) and of the local climate (as a result of changes in altitude, following movements of the earth's crust and changes in land and water surfaces) were mainly responsible for the changes in vegetation, not only its type but also its chemical composition. Modern veterinary science has shown that certain deficiencies in trace elements in soil, such as copper, molybdenum, chromium, magnesium, etc., and, therefore, also in the plants growing on such soils, may have important biological effects in animals living on those soils.

It is also known (see pp. 348 and 584) that the climate and soil affect the vitamin content of plants. In prehistoric times, before man had taken to cultivating the soil and discovered how to vary his diet, differences in the food available wherever he happened to be must have affected him in a variety of ways*.

Changes in the hydrological environment

Animals and plants living in water, whether fresh, brackish or salty, are adapted to the specific chemical and physical properties of their environment (see p. 440: Functional changes of the kidney). In other words, their nervous system and other physiological processes are habituated (see p. 242) to the specific hydrological conditions of the environment. Changes in depth, temperature, salt and oxygen content of water will require new adaptations if the previously adapted animal is to survive.

Changes in the atmospheric environment

Owing to movements of the earth's crust, the local climate and daily weather conditions of a region must have changed, not only as a result of

* Recent studies by W.W. Greulich (at the Department of Anatomy, Stanford University, California) indicate that, due to differences in diet, Japanese children in California are significantly taller, heavier and more advanced in their skeletal development than comparable children in Japan.

changes in altitude, topography and vegetation, but also because the changes in the distribution of land and sea areas are bound to bring about alterations in sea currents and movements of air masses. In view of the influence which weather and climate have on healthy and diseased organisms, such permanent climatic and meteorologic changes must have affected the physiological mechanism of the organisms living in such regions.

Changes in the surrounding biosphere

Apart from evolutionary changes, the numbers of plant and animal species in a region are liable to be affected by the continually changing surface of the earth; hence the enemies threatening the very existence of a given organism may suddenly increase or decrease. In the latter case, evolution may well progress more rapidly.

In the present section we shall only discuss the possible permanent effects of differences in weather and climate on the racial characteristics of man. This is a branch of biometeorology known as *ethnological biometeorology*

The dependence of organic life upon our atmosphere is a generally known fact. Despite its adaptive capacity, organic life is only possible within certain temperature limits. It is due to the atmosphere that the temperature on earth remains within certain limits because it acts as a heat reservoir. Without atmosphere, man would die from heat during the day and freeze to death at night time.

It was pointed out on p. 87 that without ozone in the higher atmosphere, small as its concentration is (of 1/5 p.p.m.), the ultraviolet radiation of the sun would cause sunburn at least 50 times as intense as that incurred in summer on high mountains. Nor could the eyes of animals and man have developed to their present form. Too high a concentration of ozone, on the other hand, would reduce ultraviolet radiation to below the level at which vitamin D is formed, with defective development of human and animal bone as the result.

It is our atmosphere which provides organisms with the *water* needed for their tissues and which, by eroding the soil, promotes the growth of vegetation reguired for our subsistence. It burns the millions of meteors which would otherwise collide with the earth. Without this protection all parts of the earth would be under constant bombardment by meteorites from outer space, starting fires in our forests and destroying our cities. However, in the present section we shall discuss only the possible effects of weather and climate on the evolution of life and on man in particular.

Although little scientific evidence has been collected so far concerning the continuation of changes in anatomic structures and physiological mechanisms, as a result of environmental stress, in following generations, various indirect observations seem to support this view. *E.g.*, as described on p. 295, it has been noted that oxygen stress at high altitude seems to cause permanent changes in rats, such as changes in growth and body weight, in right ventricular cardiac hypertrophy, in cardiac glycogen content, etc.

2. *Possible Physiological Changes due to Weather and Climate*

Several physiological mechanisms have been discussed in the previous sections which support the view that weather and climate may have played an important part in the evolutional changes of the living world.

(1) Prolonged thermal stress may have caused permanent changes in the *hypothalamic nuclei*, despite the fact that the body seems to be able to adapt itself to these stress conditions. The significance of thermal stress on evolution will be described below.

(2) Hypothalamic changes affect the *pituitary* functions and all the endocrinologically controlled processes of the body, such as growth, sexual activity, etc. Studies by Macfarlane and others (see p. 401) suggest a decrease in expected reproduction in tropical regions at the height of summer; in cold regions a reduction in conception rate is observed in winter. In horses various studies suggest an inverse correlation between the non-protein sulphydril concentration of the seminal fluid and the sperm mobility in the seminal fluid, or the conception rate of horses (see p. 262), which may be, at least partly, related to differences in activity of the adrenal cortex. Studies by G. Grootenhuis[3183a] in the Netherlands seem to indicate a striking correlation between conception rate percentages during the year and the hours of daylight. As daylight affects the pituitary, thyroid and adrenal glands (see previous sections), it would not be surprising to find that a relationship exists between weather, climate and fertility. Studies by Fisher, Riddle[901] and Whitman (see p. 265) suggest that, at least in pigeons, increased thyrotrophin production and thyroid activity coincides with an excess of male offspring, whereas in periods with reduced size of the thyroid, the females predominate. According to Riddle[901] and others these changing sex ratios are related to the changes in general metabolism, in particular the metabolism within the ova.

(3) Changes in production of adrenotrophin and thyrotrophin will affect the functioning of the *adrenal gland* and of the *thyroid*. On p. 263 we have discussed the great variety in potency of thyrotrophin in different species and the observation that in cold-blooded animals the quantities of thyro-

trophin produced seem to exceed those of warm-blooded animals. The possible effect of a dysfunction of the thyroid on various *malformations* of the embryo, as observed by J. Bos, J. Langman and F. van Faasen, will be discussed on p. 570.

(4) The racial differences in *metabolic* rate (due to differences in activity of the thyroid) were discussed on p. 397. Studies by Roberts and others seem to suggest that in races living near the Pole the metabolic rate is higher than for those living near the Equator.

(5) Racial differences in *17-ketosteroid secretion* as described on p. 326 may be related to changes in food and climatic stress in different parts of the world.

(6) *Plasma urea concentration* and *urea clearance* in negroes are about half of those of Europeans (see p. 393), probably another example of physiological adaptation to differences in environment.

(7) We have seen (on p. 317) that the various factors affecting the *physico-chemical state of the blood* are different in different parts of the world. In polar regions the albumin level of the blood serum is very low, the globulin level high. Blood sedimentation rates are very high. Also in many individuals in tropical and subtropical regions the globulin content is often higher than the albumin level.

(8) Factors affecting the average *blood pressure* are also apparently different in different parts of the world (see pp. 494 and 497). This is partly due to psychological factors, partly to differences in diet, but also partly the result of differences in weather stress. These differences in blood pressure will affect various physiological processes of the body *e.g.* the functioning of the kidney and its filtration mechanism (see p. 331). It may also affect the development of certain diseases (see p. 492, glaucoma incidence in China and Japan). Differences in the functioning of the autonomic nervous system alone or in combination with food differences may be reflected in differences in incidence of diseases such as arteriosclerosis.

(9) The most important developments in the evolution of life must have been the gradual changes in the functioning of the *thermoregulation system*. It is due to this system that the water-salt balance of the body could be maintained under extreme climatic conditions. Our temperature recording system, composed of a peripheral cutaneous receptor mechanism and the hypothalamic nuclei, warns the body to change its internal management. Through signals given to the pituitary, the anti-diuretic hormone is secreted in larger or smaller quantities, enabling the kidney to excrete less or more fluid or more or less salt. The development of the kidney was a momentous step in evolution, particularly during the organism's change of environment

from salt- to fresh water or to dry land. Marine invertebrates are *iso-osmotic, i.e.* their body fluids have the same salt content and osmotic pressure as the salt water in which they live. The maintenance of the salt and water balance is relatively easy. In higher animals a system was developed for the excretion of water, but without the loss of salt, and for the excretion of waste products, which cannot escape by diffusion only. In the ancestors of the vertebrates (the *Protovertebrates*) the concentration of sodium chloride in the body water was low and highly variable from river to river, from lake to lake and probably from one rainy season to the other (an interesting analysis of these problems is given by H. W. Smith.[1795a]). It was only due to the gradual development of the complex kidney structures and their controlling organs (described on pp. 331–334), that animals could live under extreme conditions in the dry and humid tropics and cold polar regions. The influence of thermal processes on evolution is also suggested by the recent observations of R.A. Boolootian at the University of California on the *effect of temperature on the determination of sex* of sea urchins and their general reproductivity as determined by geographical latitude. It seems that warm water produces more males than females; cold water has the reverse effect. Warm water, with considerably fluctuating temperatures, seems to produce a large percentage of bisexual sea urchins. Similar observations were made at the University of Cairo in 1958. Pregnant mice were separated into two groups, one of which was kept at 50° F, the other at 92° F. After 4 weeks it was found that the mice of the 50° F-group were characterized by a weight of 2/3 of an ounce, length of tail being 6.6 cm, whereas in the 92° F-group the weight was only 1/3 of an ounce, tail length 7.5 cm.

Various authors have pointed out that change in temperature may affect *embryonic development, e.g.* in amphibians. A fall in temperature causes a decrease in oxygen required for chemical processes of cell breathing, whereas oxygen diffusion is less hampered. As a result, in a multicellular embryo without blood circulation, the cells are better supplied with oxygen during periods of low temperatures. G. ten Cate[1796a] (Professor of Embryology at the University of Utrecht, The Netherlands) observed in the gastrula and neurula stage of amphibians a lower lactic acid ($CH_3CHOHCOOH$) content at low temperatures than at high ones, probably because of the higher oxygen content of the tissues at lower temperatures. In this connection the observations of Degenhardt (see p. 296) concerning malformations of the vertebral column in embryos during oxygen stress are important. Ten Cate was able to show that differences in temperature may also affect the shape of the neural plate during the period preceding the closure of the plate into the neural tube. It has also been observed that the gills in embryos are less developed at low temperatures of the environment, less branched and less supplied by blood vessels, reducing the available surface for oxygen exchange. These various experiments may explain the observations of Pasamanick and Knobloch[2682, 2683] (see p. 535) in the U.S.A. that the number of mental defectives born and the number of complications of pregnancy are significantly higher in winter than in summer, with a peak in February, even after taking into account the differences in birth rate in different months. The highest values were observed during winters preceded by very hot summers, *i.e.* during a period approximately 8–12 weeks after conception. Pasamanick and Knobloch pointed out that this is a critical period of nervous system development in the human foetus in terms of organization of the cortex. The observations of Pasamanick confirm similar observations by De Sauvage Nolting in the Netherlands during previous years (see pp. 535, refs.[2661–2675]). Another interesting effect of temperature is the influence on *cholinesterase activity*. Cholinesterase has an important function in synapses of the nervous system and its motor end-plates in muscle, preventing the accumulation of acetylcholine by splitting it into acetate and choline and therefore facilitating repetitive motor movements. In 1951 Ten Cate *et al.*[1796a] showed in amphibian embryos *(e.g. Rana esculenta)* that at a fixed morphological stage a rapid increase of cholinesterase activity occurs, which is inhibited at temperatures around 12° C as compared with embryos kept at 25° C. The *influence of seasonal changes* on the *skull* of certain mice *(Sorex araneus)* was demonstrated recently by Dehnel, Schubarth, Crowcroft and Ingels[3274]. The average height of the skull of adult animals born in February is only 4.9 mm; in June it is 6.4 mm. Similar statistically significant fluctuations were observed in the weight and length of the animal.

(10) The evolution of animal and human life at high altitudes on earth must have been greatly affected by the various physiological processes resulting from *oxygen stress* (see pp. 293-301). In particular the increased pulmonary ventilation and vital capacity of the lungs and the increased general sensibility of the nervous system may have affected both the external and internal body structure of organisms living permanently at high altitudes.

3. Evidence supporting the Assumption of Permanent Physiological Changes

It is difficult to prove that the various physiological changes described in the previous pages could have resulted in permanent anatomical and physiological adaptations, but the following considerations make it appear likely.

Geological evidence

During the earth's history, sudden evolutional changes in the animal and plant world have always been accompanied by drastic changes in the organism's environment.

Physical evidence

One of the principal laws governing energetic processes is known as the *Second Law of Thermodynamics,* in particular the *Law of Minimum Free Energy* or *Hamilton's Principle.* This law states that during irreversible processes like life, the free or available energy decreases continuously until equilibrium sets in, when the total free energy reaches a minimum. It is due to this law that a quantum fluid tends to become a globe. Unless a body in which these processes occur complies with this principle, it is bound to disintegrate as a result of external forces. In 1947, Tromp[1797a] pointed out that in all probability the same law can be applied to living organisms, the functioning of which is largely controlled by thermal energetic processes. It would therefore be surprising indeed if the thermoregulation processes in the animal body and in man did not change and adapt themselves to important permanent changes in the geophysical environment.

Mechanical evidence

According to the *Tectonic Law of Köningsberger and Hungerer* (see ref.[1797b, p. 83]), small, continuously acting forces are able to deform a body in the inorganic world (rocks, minerals, metals, etc.) plastically (*i.e.* without externally observable ruptures), if the process takes place for very long periods and provided the internal elastic limit at certain points of the body can be surpassed. The latter phenomenon is usually accompanied by micro-movements along micro-sliding planes, which in crystalline substances are determined by the space-lattice structure of the crystals. Gradual bending without fractures of a marble slab (only supported at the ends) by gravity forces, during thousands or millions of years, is a good example. In technical processes this phenomenon is known as *fatigue* of material. A piece of lime stone of Solnhofen, which requires 30,000 at. to be deformed plastically in a very short time can be plastically deformed by a force of only 1400 kg/cm^2 if the force is applied continuously for 550 days. Although these phenomena cannot be applied directly to chemically controlled processes in the living body, it is very likely that similar "plastic deformations" (see also p. 184 and 242) occur in the living organism, causing permanent changes both internally and externally, if the external forces are applied for millions of years, given that the forces surpass the internal biological limit of elasticity.

Biomathematical evidence

Studies made by Lotka[1767], Volterra[1798] and particularly Rashevsky[1779–1784] have suggested that the structure and dimensions of the different parts of the body of a living organism are not independent unities, but mathematically interrelated magnitudes. Studies in this field of *dynamic anthropometry* seem to indicate that the mathematical relations are connected with two important biological principles, the first of which is closely related to Hamilton's principle, described above. These principles, introduced by Rashevsky, are the following:

(1) *The principle of optimal design* (formerly known as the principle of maximum simplicity). This can be formulated as follows: "For a prescribed set of biological functions of given intensities, such as rate of metabolism, velocity of locomotion, etc., the design of an organism (both internally and externally) is such as to be optimal with respect to economy of material and energy expenditure". This principle enabled Rashevsky to calculate the sizes of different parts of an organism and to determine the gross shape of an organism, once the rate of metabolism and a few other physiological data are given in the mathematical formula.

(2) *The principle of organic unity.* This principle emphasizes the unity of the organism as a whole and the unity of the organic world as a whole. Therefore, any disturbance in one part of a living organism will be reflected in all the other parts, although it may be sometimes difficult to observe the changes involved. The influence of psychosomatic events on the secretion of various glands is a good example of this principle. Another aspect of this principle is known as the problem of *typology* and *personality patterns,* in recent years particularly stressed again by Sheldon[1794, 1795]. According to Sheldon and others, some major characteristics of the anatomy and outer appearance of the human body seem to be related to specific psychological patterns and susceptible to certain diseases (see p. 672).

These different aspects of mathematical anthropometry, if proved to be correct, strongly suggest that any permanent physiological change is bound to be reflected in internal and external changes of the human body.

The previous theoretical considerations make it reasonable to assume that prolonged environmental stimuli may lead to permanent evolutionary changes, which will vary for different geographical areas. Another contributory factor in the evolutionary development of animal life on earth may be the increasing variability of terrestrial climate and rate of change in the course of geological time.

The deeper biological mechanisms involved are still unknown, but the possibility cannot be ignored that they may be related to permanent changes in the chemical and physical properties and structures of the *micellar* (fluid crystal) *components of the chromosomes*. This is suggested by the artificially created heriditary changes in genetic properties produced by Avery's experiments in the U.S.A. in 1944 and more recently demonstrated by Benoit, Leroy and Vendrely in France, using nuclear cell extracts. The heriditary properties of the nucleus of the cell seem to be related to DNA (desoxyribonucleic acid or thymonucleic acid) fluid crystals, characterized by negative birefringence. The cytoplasm is rich in ribonucleic acid micellae.

4. Biometeorological Rules

Empirical studies in the field of ethnological biometeorology have taught us a number of interesting biometeorological rules which have been described by Coon[1727–1729] and others.

(1) *Gloger's Rule*: "In mammals and birds, races which inhabit warm and humid regions have more melanin pigmentation than races of the same species in cooler and drier regions; arid regions are characterized by accumulation of yellow and reddish-brown phaeomelanin pigmentation; in cold climate phaeomelanin is reduced, in extreme cases also the eumelanin (polar white)".

(2) *Bergmann's Rule:* "The smaller-sized geographic races of a species are found in the warmer parts of the ecological range, the larger-sized races in the cooler districts".

(3) *Allen's Rule*: "Protruding body-parts, such as tails, ears, bills, extremities, and so forth, are relatively shorter in the cooler parts of the range of the species than in the warmer parts.

One of the explanations of Bergmann's Rule is that the larger the body, the smaller is usually the ratio of skin surface area to bulk. As most of the heat loss takes place through the skin, a large body in a cold environment would lose less heat. Although these rules should be handled with care in the case of man, it is interesting that the average weight of Finns (according to Coon) is 154 pounds, of Spaniards 132, of Berbers of Algeria 124. In Asia the North Chinese 142, Annamites 112, Andanamese 98 pounds, Bushmen of the Kalihari 89. Needless to say, these weight differences are largely due, to differences in kind and quantity of food and general metabolism, although each of these factors is correlated (either indirectly or directly) with the average temperature condition of the region. It is nevertheless a rather interesting and practical rule that an efficient adjustment of animals to cold requires a large body mass, short extremities, much fat, deep vein-routing and high basal metabolism or a combination of these factors. Heat adjustment in nature requires small body mass, attenuated extremities (see experiments of Harrison, Morton and Weiner on the effect of high and low temperature on tail length of mice), little fat, extensive superficial vein-routing, low basal metabolism and a great number of sweat glands.

Adaptation to high altitude is usually accompanied by larger lung development, broad chests and reduced length of the body, apart from physiological changes in the composition of the blood, functioning of the heart, etc. (see p. 295). An interesting analysis of this subject was given by Monge[1622] in 1948.

5. *Influence of Weather and Climate on Civilization*

Climate and weather have affected not only the anatomy and physiology of man, but also the development of civilizations, although it is not always easy to separate the many factors involved in this process. Sears and Huntington[1750, 1752, 1754, 1755] have given a number of interesting examples of the indirect influence of climate on civilizations. For example, a few thousand years ago Indians in Western New Mexico (U.S.A.), grew maize along lakes which are at present dried out and located in a desert region. Similar cultural shifts took place in the original lake basin area near Mexico City in Mexico. During the Neolithic period, migration into the Baltic region took place at the time of a thermal maximum because the areas of optimum production of basic food plants shifted. The migration of Paleolithic man in Europe during the various interglacial and glacial periods is another example.

Huntington[1753] also stressed the significance of the psychological effect of extreme temperatures on the achievements of civilization. As indicated on p. 244, the influence on human comfort may reach a point at which the mental processes are affected. Furthermore, general motor activity is reduced to facilitate the thermoregulation of the body. This, necessarily, changes human activity, general behaviour and interest in the more serious problems of life.

Lee[1766] devoted an interesting study to the influence of climate on the economic development in the tropics, an area covering roughly 1/3 of the whole land surface of the earth, where 30% of the world's population is living. It is characterized by rather high temperatures, high humidities, heavy precipitation, frequent flooding and fairly intense sunlight evenly distributed throughout the year, but often poor in ultraviolet (despite the low geographical latitude of most of these areas) because of the high humidity and high dust content of the air in many tropical areas.

Why is it that two areas in the world with similar natural resources and racially related populations develop at a considerably different pace? Apart from political factors, according to Lee and his colleagues, four climatologically affected domains should be considered: (*i*) *Effects on plant production*: high temperature and humidity promote growth and multiplication of most plants but hasten the decay of organic material; heavy rain increases the leaching out of nutrients of the soil and wasteful erosion; it makes harvesting and storage difficult. (*ii*) *Effects on animal production*: plant forage in the humid tropics is usually low in mineral (particularly trace element) and protein content; infectious diseases and parasitism are favoured; heat stress in imported animals may reduce milk or egg production, decreases resistance to disease and may lower fertility. (*iii*) *Effects on human behaviour*: people living in the humid tropics often lack mental initiative; their accuracy at work may be affected (particularly in poorly motivated persons); the performance of a given task calls for more concentration. The occurrence and transmission of certain infectious diseases are favoured. The various physiological changes observed by Radsma were discussed on p. 242*. (*iv*) *Effects on industry*: heavy tropical rains and floods interfere with road transportation and cause many materials to deteriorate.

In a word, tropical civilizations and their cultural and economic development are usually different from those of people living in more northern latitudes. Space prevents me from discussing the subject in more detail. Readers interested in these various aspects of ethnological bioclimatology are referred to the refs.[1716-1805].

Section 5. Summary of Physiological Mechanisms Involved in Meteorotropism

The various physiological processes involved in the interaction between man and the surrounding atmosphere have been reviewed in the previous chapters (see also refs.[1806-1860]). By now the reader will be convinced of the enormous complexity of the problem and the difficulty of indicating a

* In a relatively small group of the white population, living in the humid tropics, the decreased stability of the autonomic nervous system generally observed in many European emigrants, may lead to a special disease, first described by van Wulfften Palthe[553] as *Leiodystony*. It is characterized by a general disturbance of the tonus of the unstriated muscle fibres in the whole body, causing low blood pressure and rapid changes in blood pressure, disturbances in the functioning of the heart; adrenaline causes a fall in diastolic pressure instead of an increase, etc. The many other complex clinical symptoms are fully described in the article mentioned above[553].

specific cause of a specific physiological or pathological event. Usually it is a complex of factors which determines the final outcome of weather stress.

Although probably only some of the factors involved during meteorotropic processes are known, the following summary may facilitate the analysis of factors responsible for the different meteorotropic diseases described in Part IV, Chapter 2.

Weather stress agents probably affect the body in different ways: by stimulation of the skin, of the eyes and skull (by radiation), of the internal mucous membranes of the nose, of the lungs, and of the nerves.

1. Stimulation of the Skin

Cooling or heating

This takes place three-dimensionally as convection or conduction of heat in the surrounding atmosphere or locally, due to differences in radiation of heat by the sun (see p. 336) or by the immediate, more particularly solid, environment (soil, floor or walls in buildings, etc.). The recording of these changes in environmental thermal energy is done by a hypothalamic (see pp. 232-238) and a peripheral thermoregulation mechanism (see p. 239).

The hypothalamic mechanism is located in the anterior hypothalamus (supra-optic and paraventricular nuclei), the neurons of which are able to register very small changes in temperature of the blood in the peripheral capillaries of the skin, as changes in osmotic pressure (see p. 204). According to Benzinger (see p. 234) a rise in hypothalamic temperature of only 0.01° C corresponds to an increase of one cal/sec of sweat evaporation and 0.25 ml/sec of cutaneous circulation, in other words the hypothalamus is an extremely sensitive "temperature eye" present in our brains. Studies by Magoun, Harrison and others (see p. 232) suggest that the frontal (rostral) part of the hypothalamus (particularly the optic chiasma, preoptic and supraoptic regions) controls the heat loss mechanisms (sweating, cutaneous vasodilation) and prevents overheating, whereas the posterior (caudal) part (comprising the mammillary bodies) protects against cooling.

The peripheral thermoregulation system consists of a cutaneous receptor mechanism (see p. 210), which, according to Hardy, is able to record a rise in temperature at an increasing skin temperature change rate of 0.001–0.002° C/sec, for cooling sensation 0.005–0.006° C/sec.

The changes in the rate of environmental cooling or warming depend mainly on changes in humidity, temperature and air movement of the environment as a result of influx of different air masses, weather front activity, fall or rise in barometric pressure and precipitation. Humidity, in general and in particular, rain and wind may considerably affect the temperature of the soil and walls of buildings and, therefore, the infra-red radiation received locally (see p. 37).

Owing to the close connections between hypothalamus and pituitary (see p. 203), various important hormonally controlled physiological processes are affected, such as diuresis, functioning of the thyroid (and general metabolism), adrenal gland (*e.g.* ketosteroid secretion), sexual functions, etc. (see p. 260). However, the general rate of excitation of the ortho- and parasympathetic nervous systems are also affected if the hypothalamic nuclei are stimulated.

As stated on p. 203, the posterior part of the tuber cinereum (part of the posterior hypothalamic nuclei) acts as an orthosympathetic regulation centre whereas the anterior nuclei are responsible for parasympathetic regulation. We have seen that increased orthosympathetic stimulation (or decreased parasympathetic stimulation) causes dilatation of the pupil, increases the excitability of the heart beat, increases blood pressure, causes constriction of the arterioles and capillaries of the skin, relaxes the muscles of the wall of the bronchi, increases the excitability of skeletal muscles, causes a rise in blood sugar level, decreases the coagulation time of blood, increases the red cell count, haematocrit value, haemoglobin content and plasma protein concentration of the blood and probably decreases the blood sedimentation rate, etc. This part of the autonomic system affects the adrenal gland, uterus, most arterioles and so on, more especially, whereas the parasympathetic system controls the stomach and pancreas in particular (for further details see pp. 281–283).

The final outcome of these various processes, described above, depends on a number of factors such as the past history of the organ (Law of J. Wilder, see p. 199), normal daily biological rhythms, differences in typology (physiological pattern) of the person and so forth.

The *various physiological processes* elicited as a result of cooling or heating of the environment can be summarized as follows (see p. 242): A sudden cold stress reduces the body temperature, it depresses the production of the follicle-stimulating hormone (FSH) and of other sex hormones by the anterior lobe of the pituitary; it increases the production of thyrotrophin and produces intense activity of the thyroid (and increased metabolism) by stimulating the secretion of thyroxine, causing an intense congestion of the intra-alveolar capillaries of the thyroid and disappearance of the colloid from the alveoli; it causes a parathyroid deficiency and fall in calcium and magnesium level of the blood serum; it stimulates the adrenal function and the secretion of 17-ketosteroids and increases the capillary resistance; it may reduce the function of the pancreas, but usually increases the functioning of the spleen; it elevates the respiratory rate of the liver, but reduces the metabolic rate of the kidney cortex, the fatty acid synthesis is depressed, the liver carbohydrate content is reduced; it increases the blood pressure, causes contraction of arterioles and capillaries in the skin, increases the haemoglobin, leucocyte and granulocyte content of the blood and the total protein and alubumin content of the blood serum; it decreases the blood sedimentation rate but increases diuresis and pH of urine, but lowers the chlorine excretion in urine. Experiments by Dugal and others suggest that vitamin C enhances adaptation and resistance to the effects of cold stress. Heat stress causes comparable reverse effects of cold stress. On p. 511 the influence of temperature, humidity and air movement on the acid coating of the skin will be discussed. Studies by Marchionini have demonstrated the significance of this coating as a defensive layer against microorganisms.

Radiation

As explained on p. 346, direct infrared (heat) radiation of the sun creates erythema. More important are local differences in heat radiation which may cause considerable local cooling effects (see p. 37), because the exchange of radiant heat energy between a body (the walls or floor of a room, or the soil) and its surroundings is determined by the equation:

$$H_R = \sigma E\ (T_1^4 - T_2^4)$$

The effects of ultraviolet (particularly the anti-rickets wavelength interval 302–297 mμ) were described on pp. 338-345. Photopigmentation, vitamin D and histamine formation in the skin are observed, the quantitative effects being determined by the dominating wavelength, the intensity and duration of the exposure, the altitude (above 2000 m, even wavelengths of 278 mμ may reach the skin), the specific physiological pattern of the subject (colour of hair, age, sex, part of the body, constitutional factors such as pregnancy, menstrual cycle, vegetative stigmatization), the presence of photodynamic substances (see p. 350), etc. The influence of vit. D on calcium and phosphate metabolism, hibernation, thyroid function and general metabolism will be discussed on p. 584.

Indirect results of irradiation of the skin with erythema-producing doses of sunlight are increased gastric secretion (over-exposure may even produce gastritis, see also p. 339), fall in blood pressure, increase in number of erythrocytes, haemoglobin values, calcium and phosphate level of the serum, increased protein metabolism. On p. 518 the lethal effect on micro-organisms will be discussed and the significance of the 60% relative humidity boundary of the air during irradiation.

Ultraviolet deficiency causes a thyroid hyperplasia, colloid loss and high iodine content of the thyroid (low iodine blood serum level), increase in size of the parathyroid, softening of the bones, etc. (see pp. 273 and 276). As indicated on p. 339, excess of solar radiation, particularly at great altitude or at the seacoast (see p. 643), may cause overstimulation of the thermoregulation mechanism, nervousness, loss of appetite, nausea, fatigue, head ache, insomnia, etc.

2. Stimulation of the Eyes and Skull by Radiation

Over-exposure of the eyes to *infrared* and *ultraviolet* radiation may cause inflammation of the conjunctiva and cornea and formation of cataracts (*i.e.* opacity of the eye lens). *Visible light* (λ = 380–780 mμ) affects the pituitary function according to Benoit (see p. 347), probably by stimulating the optic nerves and optic chiasma and the neighbouring hypothalamic nuclei or by stimulating the peripheral thermoregulation system in the skin of the human skull. On p. 542 the effect of lightflashes on the central nervous system has been described. A frequency of 10–16/sec may cause epileptic seizures, whereas other frequencies may have favourable effects.

3. Stimulation of the Internal Mucous Membranes of the Nose

Several mechanisms may be involved.

(1) *Stimulation of the olfactory nerves* by volatile substances in the air, which may cause a stimulation of the different parts of the rhinencephalon (see p. 302): the smell-perception area, areas mediating the unconscious-emotional life (including the moods) and areas mediating certain somatomotor, cardio-vasomotor, visceral and endocrinal activities.

(2) Changes in *permeability of the mucous membranes* to various chemical and organic substances (see p. 335).

(3) *Allergic reactions with allergens in the air* (see p. 460).

4. Stimulation of the Lungs (both Electrostatic and Chemical)

Various biometeorological agents seem to affect the body through our lungs. The most important mechanisms seem to be: stimulation by natural ions of the air, by trace substances in the atmosphere, by air-polluting substances, by reduced partial oxygen pressure and by thermal stress.

Stimulation by natural ions of the air

Krueger, Smith and Beckett (see p. 357) were able to show that a surplus of positive ions of the air (concentrations comparable with those observed in nature) cause an increased irritability of the mammalian tracheal mucosa, decreased ciliary rate*, contraction of the membranous posterior wall of the trachea (a process which could be reversed by negative ions), dryness of the mucosal surface and vulnerability of the cilia of the trachea to mechanical trauma. Breathing of 35 l/min under normal conditions drops to 25 l/min after preliminary exposure to positive air ions. High densities of positive ions may produce dryness, burning and itching of the nose, nasal obstruction, headache, dry scratchy throat, itching of the eyes, etc.

The effect of positive air ions seems to be due to positively ionized carbon dioxide, that of negative air ions to negatively ionized oxygen. The biological effects seem to be related to the effect of these ions on the intra-cellular respiratory enzymes. Positive ions seem to release serotonin (see p. 364) in the trachea cells, which causes contraction of the smooth muscles and vasoconstriction in the tracheal wall. In the presence of negative ions serotonin would be quickly oxidized.

Stimulation by trace substances in the atmosphere

The significance of ozone was discussed on pp. 88-93. Small amounts in heavily polluted areas oxidize the hydrocarbons in the atmosphere into peroxides, aldehydes, nitric acids, etc., substances which are responsible for the irritation of the membranes of nose and throat. The ozone can be formed in the lower parts of the atmosphere by sunlight (waves shorter than 3600 Å), in the presence of organic substances, out of NO_2 (see p. 90). It may reach the earth's surface by turbulent air currents carrying the ozone downwards from great heights.

It was pointed out on p. 89 that thunder or snowstorms, influx of polar maritime air masses and the rear part of depressions are important factors in the increase of ozone in the air (normally 20–30 γ/m^3).

Large concentrations of ozone (above 2000 γ/m^3), produced under specific

* *Negative* air ions increase an initial ciliary rate of 1400–1500 beats/min (in rabbits) by about 200 beats/min (reaching a maximum after 10–20 min), while *positive* air ions lower the rate by 300 beats/min or abolish ciliary activity altogether. The minimal ion densities producing changes in ciliary activity in rabbits, within 30 min, are $2.5 \cdot 10^3$ ions/cm²/sec for negative ions, $1 \cdot 10^4 - 2.5 \cdot 10^5$ ions/cm²/sec for positive ions. Negative ions have no effect in N_2 or CO_2, but in O_2 or cigarette smoke the rise in ciliary rate is the same as in ordinary air. Positive ions have no effect in N_2 or O_2, but in CO_2 or cigarette smoke the lowering of the ciliary rate takes place more rapidly (within 2–5 min). N_2, O_2 or CO_2 by themselves have no effect on ciliary rate. Cigarette smoke alone promptly decreases the ciliary rate by about 200 beats/min.

microclimatic conditions, may cause serious inflammation of the respiratory tract; it lowers the resistance to respiratory infections; the O_2-uptake and CO_2-output are decreased; it may diminish general metabolism (lowering the body temperature, see pp. 91 and 212). In small quantities it stimulates the olfactory nerves and the rhinencephalon (see p. 302). Concentrations of 30-90 γ/m^3 seem to increase the potassium level of the blood and to decrease the calcium level.

Stimulation by air-polluting substances

(1) *Air-polluting gases.* Various hydrocarbons and other irritating gases (produced by soil gases, factories, etc., see p. 96) may cause overstimulation of the olfactory nerves (and rhinencephalon) in people living in such air-polluted areas. Diesel engines in road traffic produce large amounts of soot and other odorous substances which are irritating to the mucous membranes of throat and nose and increase smog conditions at low level in the atmosphere. High concentrations of CO in heavy petrol-driven road traffic also have noxious effects. The carcinogenic properties of 3,4-benzpyrene, a substance produced chiefly by the not heavily loaded, slowly running petrol engine, was discussed on p. 97. It is decomposed by ozone and sunlight. SO_2 in the air in concentrations of 1–8 ppm may increase the pulse and respiratory rates and the tidal volume; it may cause a chronic inflammation of the upper respiratory tract. High concentrations seem to inhibit ciliar activity (see p. 499) of the trachea. According to Heinke and Hermann (see p. 99), increased acidity of the air increases the acidity of the skin and therefore strengthens the acid coating of the skin, this acting as a protective layer against bacteria and fungi which might otherwise bring on eczema. According to Cauer, very low pH-values (less than 2.7) are commonly observed at high altitudes, which may be one of the causes of the favourable effect of high altitude on several types of eczema.

(2) *Air-polluting particles and aerosols* (particles of 2 mμ–5μ). The biological effect of *organic* air-pollutant particles, pollen, spores, etc. (see p. 106) on allergic patients will be discussed in detail on p. 460. *Inorganic* particles (soil minerals, brick dust, etc.) with their electrostatic charges may be deposited on our skin or hair, but may penetrate into the lungs if the particles are less than 10 μ in diameter, those reaching the lower bronchi being usually less than 3 μ. Up to 90% of aerosols, with many particles of 0.1 μ, each with a great number of elementary charges, may remain in the lungs and may cause diseases such as silicosis, siderosis, anthracosis and so forth (see p. 113). The possible genetic effects of air pollution were briefly mentioned on p. 114. The relatively small mass of aerosol particles, as com-

pared with their surface, considerably accelerates all physico-chemical reactions between the aerosol substances and the lung tissue. With decreasing size of the particles of the aerosol clouds the total surface of the particles increases and therefore the speed of the chemical reaction. Decreased atmospheric pressure at higher altitudes facilitates the penetration of aerosols and strengthens the physico-chemical reactions in the lungs.

Stimulation by reduced partial oxygen pressure

Various physiological effects of oxygen stress, such as increased pulmonary ventilation, vital capacity and CO_2 elimination of the lungs, heart and pulse rate, blood pressure, blood-circulation in long capillaries, blood volume, blood cell count, haemoglobin, leucocytes, thrombocytes, fibrinogen, adrenal activity (*e.g.* 17-ketosteroids), water retention, peripheral capillary resistance, general sensibility of the nervous system (lowered rheobase for taste, tactile and eye stimulation) were reviewed on pp. 293 and 298. Eosinophils and prothrombin contents of the blood decrease, the smooth muscle fibres of the bronchi dilate, the intra-ocular pressure decreases. Permanent oxygen stress may cause the body weight of growing animals to be significantly lower than normal, cardiac hyperthrophy is common, liver and muscle glycogen decrease, the weight of adrenals increases and that of the thymus decreases.

More extreme oxygen stress during pregnancy may cause malformations of the vertebral column, the degree of malformation depending on the rate of oxygen deficiency and the day that the stress occurred during the period of pregnancy. The latter factor also determines the site of the malformation. The effect is reduced by vitamin E.

Stimulation by thermal stress

Excessive heat of the whole body increases pulmonary ventilation (see p. 297). Cold stress increases oxygen consumption. Warm air increases the permeability of the nose and lung membranes and facilitates the penetration of foreign substances, also the oxygen intake and CO_2 release of the lung membranes.

5. *Direct Stimulation of the Nerves*

Possible effect of electrostatic and electromagnetic fields

Although the evidence for a direct stimulation of the nerves (or brain centres) of the body by the electric fields in the atmosphere is still very scanty, a number of observations point strongly to a direct influence.

Although electrostatic fields usually do not penetrate into buildings, almost everyone is probably exposed to the fluctuating potential gradient and electromagnetic fields in the atmosphere outside buildings at least part of the day (see pp. 74 and 79).

The principal evidence for a direct effect of the pulsating electrostatic fields or electromagnetic alternating fields in the atmosphere on the living organism is supported by the observation of Schua in 1952, who demonstrated a sensitivity of golden hamsters to alternating fields of 900 V/m and a few c/sec frequency (see ref.[35]), and of bees to thunderstorms (see ref.[34]). Previously, in 1936, Saito had shown that rabbits placed between an electromagnet become restless after 8-10 minutes, the capillary vessels being dilated. Contraction of the pupils was observed in rats, suggesting parasympathetic stimulation.

Reiter showed in 1953 that the pH of subcutaneous tissue in guinea-pigs would change if the animals were placed between plates 1 m apart with alternating fields of 50–100 Hz frequency. Similar observations were made during thunderstorms. If the animals were placed in a metal cage of Faraday, no changes in pH were observed.

Gengerelli and Holter showed in 1941 that frogs' nerves placed in an alternating field of 10,000 V and 60 c/sec contract, provided the nerve be not surrounded by a saline solution. Similar observations were made by Hermann as far back as 1887.

Experiments by Thompson, Dunlap and others, since 1910, indicate that rapid contractions of the eye muscle occur if the head of a person is surrounded by electric wires creating alternating electromagnetic fields with a 60 c/sec frequency. Owing to these muscle contractions, the subject experiences flickering of the eye. Prolonged experiments even brought on headaches. These and many similar experiments support the view that strong electromagnetic fields in the atmosphere, within certain frequency intervals, may have important biological effects on the nervous system of man and animals*.

Possible effect of natural changes in atmospheric pressure

On p. 50 it was pointed out that during heavy storms in W. Europe, as a result of approaching low-pressure areas, changes in barometric pressure of 40 mm are not uncommon. In the case of approaching typhoons, differences of 90–100 mm can be observed (with pressures in the centre of a typhoon of 880 millibar or 660 mm).

* Recent studies by Else Haine and H. König (*Z. angew. Entomol.*, 47, 4, 459–463 (1960) have shown that moulting of the aphid *Myzus persicae* Sulz. was low when electromagnetic waves of 9 c/s and high intensities were applied; moulting increased with medium intensities.

The experiments of Smith and Bouchard were described on p. 297, indicating that if the atmospheric pressure drops 26 to 98 mm, in 12 to 48 hours, water retention takes place in the body accompanied by restlessness. If further experiments were to confirm this observation, it seems very likely that a direct atmospheric pressure effect can be expected as a result of the approach of very active low pressure areas.

Possible effect of microseismic vibrations

On p. 212 we described the *Rohracher effect, i.e.* the mechanical microvibrations of the human body with frequencies of 6–12/sec. and amplitudes of 1–5 μ (up to 50 μ with tensed muscles). The frequency increases with increased thyroid activity. Recent experiments by Deelder (biologist of the Fishery Research Institute at IJmuiden, the Netherlands) on the silvereel *(Anguilla anguilla)* indicate that these animals are able to register approaching active low pressure areas (storm centres) even in an aquarium located in a dark cellar of the institute. Weather analysis suggests that this form of meteorotropism is not due to the differences in atmospheric pressure or other obvious meteorological factors. Apparently the eel reacts to the microseismic vibrations of the earth's crust caused by such storm centres*. If the facts of these studies can be confirmed, we shall have to allow for the possibility of a similar effect on human microvibrations.

Although most of the biometeorological factors described are particularly active outside buildings, the various observations described on p. 82 clearly indicate that an intimate relationship exists between the local microclimate in rooms and buildings and the external macroclimate. Several of the biometeorological effects described will therefore be observed in persons both in and outside buildings; all the more so in view of the observed close relationship between weather, diuresis and 17-ketosteroid secretion (see p. 328), even if the subject has been outside the building in which he lives for an hour or less per day.

Apart from the fact that the biological effect of each of the described weather stresses will be different, depending on the sex, age, typology, past history of the subject (Law of Wilder), biological rhythm and period of the

* In Holland such micro-seisms have amplitudes of 1–20 μ, frequencies of 6–8 sec (with depressions over the Atlantic) or about 2 sec (over the North Sea). Careful analysis by Deelder has shown that the number of migrating eels rises sharply after the occurrence of micro-seisms with a frequency of about 3 sec. In fact, so far never 3-second micro-seisms have occurred without being followed by a distinct increase in catches, a conclusion based on 1000 fishing days. Calculations by the Dutch seismologist Veldkamp indicate, that micro-seisms with a frequency of 4 sec and amplitude of 7 μ cause pressure fluctuations at the base of a 10 m water column of 2 dynes/cm^2.

year, we have seen that the living organism has a great capacity for adapting itself to continuous stress conditions.

On p. 199 it was pointed out that the excitability of both nerves and muscles will increase with continued stimulation till a certain maximum is reached, after which the nerve or muscle tends to return to its resting value, known as *accommodation* in nerves, *fatigue* in muscles. But also in the case of more complex stimuli gradual changes in the response to those stimuli are observed, a process described as *habituation*.

The terms *adaptation* and *acclimatization* are used for habituation to temperature stress of the environment. All these processes are probably due to permanent changes which take place in the points of contact (synapses) between the individual neurons. As a result, the response of the neurons to the same stimulus will change continuously. Considerable evidence for this theory has been put forward by Eccles[485], Glaser[631, 632], Konorski[508], Young[560] and others. In view of the foregoing considerations, it will be obvious that it is extremely difficult to predict the outcome of a specific weather stress on a particular person in a certain period of the year. However, now that effect of the individual meteorological factors is better understood, the differences between the biological effect of land and sea climate (see p. 26) and mountain climate (see p. 27) can be analysed more scientifically.

In the following Chapter of Part IV, on the biometeorological effect of weather and climate on diseases, the various general principles summarized in this section will be more fully applied.

CHAPTER 2

Biometeorological Effect on Diseases (Pathological Biometeorology)

In the previous sections of Part IV a considerable body of evidence was produced of the many physiological changes that take place in healthy man as a result of changes in climate and weather in our environment. Although in theory similar relationships should be detectable in human pathology, it has been suprisingly difficult so far to establish *"causal"* relationships between specific weather conditions and certain diseases with certainty.

The vast amount of literature in the field of pathological biometeorology (see refs.[1861–3403]) indicates that many *"statistical"* relationships have been found, a great number of which have proved to be highly significant from a mathematical point of view. However, the exact causal relationships have only been established in a relatively small number of cases and considerable research is required to solve the many open questions.

A complete review of all the discovered statistical relationships between weather and climate would call for a volume to it self. In the following sections only a comparatively small number of studies will be briefly reviewed. Clinicians, interested in bioclimatological studies of a specific disease, are recommended to read the original publications given in the above-mentioned references and to study in particular the publications by Petersen[16], De Rudder[6], Assmann[1], Menger[12] and Mücher[15].

In this Chapter the various problems related to pathological bioclimato- will be discussed in five different sections, *viz.*,

(1) *General pathological biometeorology* (divided into: Principal meteorotropic diseases, Miscellaneous meteorotropic diseases, and Important meteorotropic clinical phenomena). The observed weather--disease relationships in eight principal groups of meteorotropic diseases are reviewed, followed by a brief discussion of miscellaneous diseases and a group of important clinical phenomena such as mortality, fertility, birth frequency and so on.

(2) *Seasonal pathology.* A brief review is given of the observed seasonal changes in normal physiological processes in healthy man and in the incidence of various diseases.

(3) *Influence of weather, climate and season on pharmacological treatments* A brief summary of published studies on the influence of weather on the effect of specific pharmacological treatments is followed by an extensive review by Dr. S. Renaud of Canada on the effect of stress conditions in general (and, therefore, also weather stress) on drug absorption, the physiological action and the toxicity of drugs. This rather neglected field in clinical medicine is most important, because the studies referred to will clearly show that the same drug applied during different weather or seasonal conditions may have entirely different clinical results.

(4) *Influence of climate on the geographical distribution of diseases.* In this section by Dr. J. M. May (U.S.A.) another interesting aspect of pathological biometeorology will be discussed, *viz.,* the influence of weather and climate on the distribution of diseases in the various countries and Continents.

(5) *Climatotherapy.* Finally, the practical applications of the observed relationships between weather and normal physiological and pathological processes to the treatment of various diseases are discussed, what is known as climatotherapy. Of this vast and still insufficiently developed subject the principles and methods of aerosol, thermo-, helio-, climatic chamber, thalasso- and balneo-climatological treatments will be briefly reviewed in order to stimulate future research in this new and most promising approach of modern clinical treatment.

Sect. 1A. General Pathological Biometeorology (Principal Meteorotropic Diseases)

Subsect. A. ALLERGIC DISEASES[1861-2177]

Only the following three aspects of this complex problem will be briefly discussed in this subsection: the general physiological principles involved in allergy; weather climate and hayfever; weather, climate and bronchial asthma. Some meteorotropic allergic skin diseases will be dealt with on p. 563.

*1. General Physiological Principles Involved in Allergy**

Allergy is a phenomenon which can be defined as altered reactivity of an

* Students of biometeorology are referred to the textbooks on allergy, some of which are: R. A. Cooke, *Allergy in Theory and Practice* (W. B. Saunders, Comp., Philadelphia, 1947); K. Hansen, *Allergie* (Georg Thieme Verlag, Stuttgart, 1957); J. M. Sheldon, R .G. Lovell and K. P. Mathews, *A Manual of Clinical Allergy* (W. B. Saunders, Comp., Philadelphia, 1947).

individual to a specific substance, usually resulting from prior experience with the same or a chemically related substance.

A state of altered reactivity which is characterized by increased susceptibility to a protein or toxin, following ingestion or injection of the protein, or to infection by a toxin-forming disease, is known as *anaphylaxis,* described for the first time by Richet in 1902. This process is the opposite of the usual immune state following toxin injections.

The altered reactivity or allergic reaction is explained as an antigen-antibody reaction. An *antigen* is any substance (usually a protein), normally not present in the body, which, when introduced parenterally (*i.e.* otherwise than through the alimentary canal) into the blood-stream or animal tissues, stimulates production in the body of a substance, described as *antibody,* and which, when mixed with that antibody, reacts specifically with it in some observable way. It is found that most likely antibodies are modified *serum globulins,* in particular those resembling γ-globulins.

Various theories have been put forward to explain the antibody formation. Breine and Haurowitz[1860a] assumed that the antigen, or fragments of it, penetrates the site of globulin synthesis (see pp. 286 and 268) and causes a slight change in the globulin molecules produced. The globulins, like all proteins, are characterised by complex amino-acid structures. Small structural changes may affect the chemical properties considerably. If these new molecules enter the blood-stream and meet the antigen, the globulins may be sufficiently modified to react with the antigen. The antibodies and antigens are assumed to be multivalent, having at least two immunologically reactive groups on them, which accounts for their exquisite specificity of action. Some variants of this theory have been put forward; *e.g.* by S. Mudd, L. Pauling, F. M. Burnet, F. Sabin and others. In view of the influence of the thyroid gland on the globulin level of the bloodserum (see p. 268), this factor should also be taken into consideration.

If the allergic reaction occurs fairly spontaneously, it is called *atopy,* after Coca. This hypersensitivity is often found to run in families.

As a rule protein-antigens are deprived of their antigenicity when broken down by acid hydrolysis or by the action of proteolytic enzymes, such as those present in the gastro-intestinal tract. Therefore most antigens act only if absorbed by the body parenterally. However, certain food proteins, even in minute quantities, keep their allergic properties.

Eosinophilic granulation in tissue cells and white blood corpuscles is often considered to be an evidence of allergic response. As considerable fluctuations in the blood count may occur as a result of ordinary weather stress (see p. 284), however, eosinophilia is not necessarily a sign of allergy.

Various types of environmental allergens are known. According to the route through which they produce an allergic reaction they are classified as inhalants, ingestants, contactants, etc. Examples of allergens are pollen, house-dust (particularly the finest fractions passing through sieves with a mesh of 76 μ), mould spores, bacteria, poison ivy, certain foods or drugs, etc.

A considerable amount of literature has been published on the possible influence of *house-dust* on bronchial asthma and other allergic phenomena. Harsh[1885], Maunsell [1896] and others assumed that the allergenic properties increase with increasing humidity of the atmosphere. Harsh attributes this to the increased action of microorganisms on certain constituents of dust during humid weather. Maunsell believes that humidity favours fungi development. The fungi break down the house-dust and decompose wool, feathers, paper and so forth. Other microorganisms may join in this process. As a result a house-dust antigen could be formed, from several sources. Some observations make the validity of this house-dust theory doubtful: (*i*) Although in two areas the locally collected house-dust gives a positive cutaneous reacion (see below), one area may be free of asthma, whereas in the other area it is very common; (*ii*) The same house-dust extract may produce entirely different reactions at different times of the year (see p. 198); (*iii*) During warm and very humid periods, *e.g.* as a result of the influx of warm tropical air with heavy rain, the incidence of asthma is very low. The same is true in the Netherlands during foggy periods.

A skin test is often applied in order to establish a possible source of allergic reaction in the body. In the *scratch method* the supposedly allergenic material is gently rubbed with a sterile needle into a superficial scratch in the skin (usually performed on the flexor surface of the forearm in adults and the back in infants and young children). The skin is cleansed with 70% alcohol prior to the test. In the *intracutaneous* test about 0.01 ml of the allergenic extract is injected into the superficial layers of the skin. This produces a *wheal* (*i.e.* a transient, circumscribed, red-white elevation of the skin) about the size of a large pin-head. In a *positive cutaneous test,* so called, the wheal is enlarged, with an irregular outline surrounded by an erythema and often accompanied by itching. The wheal is compared with a control, *i.e.* a similar injection nearby with only the sterile extracting fluid.

Usually the following diseases are included among allergic diseases: *asthma, allergic rhinitis* (*i.e.* inflammation of the nasal mucous membrane) of the perennial and seasonal *(hay-fever)* type, *urticaria* (a condition marked by the appearance of red-white elevations of the skin, accompanied by intense itching, persisting for hours or days), *allergic dermatitis* and allied *dermatoses*, etc.

2. *Hay-fever*[1923–2177]

Hay-fever, pollinosis or *seasonal vasomotor rhinitis* is a seasonal form of allergic rhinitis caused by pollen or mould spores. The term "hay-fever" is actually incorrect, because the clinical symptoms are never caused by hay but by seasonal allergens produced by plants, usually flowering around the hay season.

Characteristic symptoms are: excessive sneezing, stuffiness and intermittent, profuse, clear, watery nasal discharge. Temperature elevation is very rare, secretion of tears and itching of the eyes are common; also itching of the nose, roof of the mouth and posterior pharynx are reported. Dull frontal headaches and a feeling of fullness over the paranasal sinuses are common. Some patients complain of general fatigue, depression or irritability. Anatomical symptons are: hyperplasia of the epithelium, oedema, eosinophilic infiltration and connective tissue proliferation of the submucosal tissues, hyperplasia and dilatation of the mucous glands, frequent dilatation of the blood vessels.

Hay-fever symptoms unassociated with seasonal phenomena and usually caused by house-dust, animal products (hair, feathers, etc.) or foods, are called *allergic rhinitis*. If no allergic agent can be demonstrated, the clinical symptoms are described as *vasomotor rhinitis*. It is probably due to instability of the autonomic nervous system regulating the blood flow in the nasal mucosa. Slight cooling effects, emotional trauma, fatigue, etc. could create these ostensible symptoms of hay-fever.

As pollen, mould spores, house-dust and most other allergens in our environment are light substances, which require only slight air turbulence to become floating particles in the air, it is evident that meteorological factors must control to a considerable extent the distribution and quantity of pollen and spores in the atmosphere (see pp. 106-111) and must therefore affect the incidence of hay-fever attacks. In view of the interrelationship between the internal micro-climate of rooms and buildings and external weather conditions (see p. 82), hay-fever patients in closed buildings and rooms will also, obviously, experience these various factors. The study made in 1896 by Maunsell of this matter is illuminating. The concentration of airborne spores in the air of undisturbed bedrooms in London proved to be the same as occurred in the adjacent outdoor atmosphere in London.

The similarity between vasomotor rhinitis and ordinary hay-fever, the disappearance of hay-fever symptoms in certain patients even during the pollen season after climatic chamber treatments (see p. 640) and the experiments of Hansen and Michenfelder[2045] (see p. 198), supported by the studies of Takino in Japan, strongly suggest that disturbances of the autonomic nervous system as a result of weather stress (see p. 195) may play a more important part in this whole phenomenon than is generally assumed by most allergists. They are inclined to concentrate their treatment on *hyposensitization, i.e.* serial injection of increasing amounts of one allergen or mixtures of related allergens.

The observation made by Cooke and others in the U.S.A. to the effect that a substantial group of patients display their severest symptoms from the middle of September to the middle or end of October, when all known pollens or moulds are declining or may even be absent, underlines the influence of other non-allergenic factors. These patients give ragweed reactions (see below) and may improve during August and early September after treatment with ragweed extracts, but get worse at the end of September or October. Others give no reaction to any of the known pollens. A variety of reasons have been suggested in the past to account for this phenomenon, such as returning from holidays to re-painted apartments in the city and the like. But many people are afflicted year after year, irrespective of such occasional incidentals like re-decoration of apartments. In view of the weather correlations established for bronchial asthma (see p. 467), there seems to be little doubt that, apart from allergens, other weather-stress phenomena are important factors in the causation of pollinosis.

According to Cooke (U.S.A.) there are three main pollen seasons, *viz.*, (*i*) *Spring* (from early March to June): Tree pollen of elm, poplar, ash, beech, birch, oak, sycamore and hickory (in this order of appearance) is responsible for certain hay-fever symptoms. As the time of onset and quantity of pollen produced by these trees are greatly influenced by the weather in the previous weeks, a definite meteorotropic correlation can usually be found. (*ii*) *Early season* (mid-May to first week in June, with a maximum in the last week of May): Pollination of plantain and sorrel is common. Grasses start pollinating feebly in the U.S.A. in mid-May, continuing until the middle or end of July, clinical symptoms usually beginning around 30th May (in the Netherlands about 15th May). (*iii*) *Late season* (early August until first frost): The main allergic agents are the ragweed pollen (high and low). These high ragweed pollens reach a maximum usually around 25th to 30th August, the low ragweeds around the first two weeks of September.

Readers interested in further details of this problem are referred to the references[1923-2177] and the various textbooks on allergy.

3. *Bronchial Asthma*[1863-1922]

Definition and classification

The word asthma was used originally as a synonym for breathlessness or gasping. At present it is used to indicate recurrent paroxysmal dyspnoea, accompanied by a wheezing cough and a sense of constriction, which can be caused by heart diseases *(cardiac asthma)* or renal diseases *(renal asthma)* or may be due to a certain allergy of the bronchi, known as *bronchial asthma*. The latter form of asthma is a typical meteorotropic disease, although most physicians still consider the main cause of dyspnoea either to be the result of infections of the respiratory tract (causing a bacterial allergy known as *infective asthma*; see physiological mechanism described below), of non-infective allergens (inhalants, food drugs, therapeutic serums, etc. causing the formation of antibodies in the bronchial mucous membrane), of psycho-somatic factors *(psycho-somatic asthma)* or of deficiency in certain endrocrinal functions *(endocrinal asthma)*. It will be shown in the following section that each of these four factors, including weather stress, may bring on an attack of asthma; but it is by studying the observed asthma–weather relationship that the deeper physiological mechanism of this disease comes to be better understood.

Physiological characteristics of bronchial asthma

The dyspnoea in the case of bronchial asthma usually begins with *wheezing*, sibilant and sonorous râles being heard throughout the chest, followed by tightness in the chest and increasing degrees of breathlessness. The dyspnoea is caused by bronchial and, especially, bronchiolar obstruction as a result of contraction of the constrictor fibres of the smooth muscles of the bronchi, initiated by a reflex stimulation of the parasympathetic nervous system or by substances like histamine, which may be locally liberated as a result of bronchial infection. It is assumed that the penetration of a specific antigenic protein creates certain antibodies. The reaction between both may liberate certain toxic substances which damage the cells in which they appear, one of the results of this damage being the liberation of histamine. The spasm of the small bronchioles leads to an extreme degree of emphysema. In chronic asthmatics hyperdistension of the lungs can be observed, the bronchial tree being filled with tenaceous mucus, the smooth muscles being hypertrophic.

The dyspnoea may occur as intermittent attacks in asthma patients or be continuous with exacerbations of varying degree. A condition of severe and continuous attacks is known as *status asthmaticus*. On the basis of the incidence of asthma attacks, asthmatic patients can be classified into two groups: one group shows pronounced peaks in the degree of asthma attacks, both short-term and long-term (seasonal) fluctuations; a second group, also indicated as *non-atopic asthmatics*, are characterized by a lack of seasonal increase in asthma in the late summer and autumn; they do not exhibit clear skin tests with allergens. This group of asthmatics is found more especially among people above the age of 50. Endocrinal and cardiac disturbances are common within this group.

Physiological studies of asthmatics revealed, apart from differences in the functioning of the lung*, a number of characteristic differences compared with normal persons of the same age and sex.

(1) The average *haemoglobin content* of the blood in asthmatics is often considerably higher than normal. Values above 100% (*i.e.* 16.0 g%) are quite common.

(2) The average *blood pressure* is often low.

(3) The *17-ketosteroid secretion*, particularly in young asthmatics, is often very low (see p. 326). According to Zimmermann (see p. 516), this is accompanied by decreased resistance to infections.

(4) *Acidity of the blood and urine* decreases considerably (pH increases) shortly before the asthma attack begins (see also p. 193). After the attack, the pH decreases rapidly. According to Tiefensee, acid vapours have favourable effects on asthmatics (see p. 99).

(5) Haury[1885a] studied the *magnesium level* of the blood (see p. 276) of asthmatics. About 50% of the patients, during an asthma attack, have a lowered magnesium level (hypomagnesia), *i.e.* 1.1–1.7 mg/100 cc as against 2.33 in normal persons of the same age group. As magnesium deficiency may cause muscular spasms and convulsions, it may be a contributing aetiological factor of asthma. According to Haury, Rosella and Plá, injections of 20 cc of 10% magnesium sulphate (injected slowly intravenously) during serious attacks bring immediate relief.

(6) Preliminary studies by Tromp suggest an inefficient *thermoregulation system* of asthmatics (see p. 253). The observed meteorotropic relationships, described in the section below, are in agreement with these differences in the physiological pattern of asthmatics.

* One of the characteristic features is the difference in *vital capacity* of the lungs, *i.e.* the amount of air exhaled in a maximum expiration after a maximum inspiration. This figure is fairly constant for a healthy individual. It depends on health, size, weight, age and sex.

Studies by Feinberg in Chicago in 1929 indicated that the vital capacity is reduced during asthma attacks proportional to the severity of the latter. The average vital capacity between attacks was considerably reduced in adults but very little altered in children.

Incidence of bronchial asthma

Few accurate data are available in different countries, but the following figures seem to represent a minimum value: A large-scale survey in the Netherlands by Doeleman in 1955 indicates that the incidence of asthma among children of 6–14 years of age is 6 per 1000; for the total population this figure may be 9 per 1000. According to Collins, in 1935 the incidence for this age group in the U.S.A. was 4 per 1000. In Glasgow (Scotland), in 1953 an incidence of 3 per 1000 was found among children from 4–18 years. In Sweden (in 1948–1950), for the age group 7–14, the figure was 7 per 1000. In Stockholm itself it was almost 14 per 1000. These figures clearly indicate the social significance of bronchial asthma and the necessity of studying the influence of weather and climate on asthma as a preliminary to developing certain climatotherapeutic methods.

Biometeorological studies

As will be apparent from the refs.[1863–1922], many authors have studied the direct effect of weather and climate on bronchial asthma. Although several studies suggest a statistically significant relationship with certain weather conditions, the clinical material used for these studies was not very extensive as a rule and the methods were not sufficiently standardized to allow of a clear-cut statistical analysis.

The first facilities for studying the biometeorological aspects of asthma on a big scale were created by Schook in 1953 at the Asthma Centre "Heideheuvel" of Hilversum (the Netherlands). The clinical data collected by Schook and his assistants have been analysed by Tromp since 1955. As the methods applied can be used for other biometeorological studies, a fuller discussion of the methods and results would seem to be warranted. Since 1953 a fairly constant group of children has been daily observed at Hilversum and the degree of complaints is recorded (see Fig. 33 on p. 167). The children go to a school near by but live and eat at the Asthma Centre Here they sleep in 4 resisdences, *i.e.* 3 for boys of 11–13, 12–14, 17–18 and one for girls of 10–20. A number of children of the same age group share a bedroom. There are about 25 boys in the youngest group. Twenty-one of 12–14, twenty-one of 17–18 and twenty-eight girls, making a total of about 95. During holidays (of which strict note is kept) the total number may decrease to 20-30. Apart from clinical observations, all psychosomatic disturbing factors (festivities, visits of parents, etc.) are recorded. At 6 p.m. the sister or physician, who has been observing the children during the day, makes a short asthma report. In these lists the complaints are indicated as follows: no complaints (value = 0), wheezy (usually a whistling breath = 1), slightly breathless (=2), breathless (=3), very breathless (=4). With these data a day-to-day check can be kept of the percentage of children suffering from an attack of asthma (*i.e.* complaints 2 or higher) and of the average degree of attack. These records are kept for each residence separately, and for the total number of children.

A similar study is made of adult asthmatic patients. Former patients of the Oto-Rhino-Laryngological Department of the University Medical Centre at Leiden are requested to fill in daily complaint charts. Whereas the "Heideheuvel" data are based on entirely objective observations, this adult group provides subjective data. This disadvantage notwithstanding, the complaints of this adult group were found to tally pretty well with the children's. All the daily clinical and meteorological data of the seven-year period 1953–1960 have been compiled in a great number of charts, an example of which is reproduced in the Figs. 31 (p. 163) and 84.

An analysis of the 7 years of data collected by Schook at Hilversum has shown the following weather-asthma relationships:

(1) Periods of high and low percentages of asthma occur *every month*, the periods varying in length from a few days to a week or even 10 days.

(2) *Every year* the same pseudo-seasonal rhythm of asthma frequency is observed, both in the children at Hilversum and the adults at Leyden. In winter and early spring the asthma frequency is low; it is high in summer and particularly so in autumn.

(3) The fluctuations in the *daily amplitudes* of asthma frequency usually increase abruptly at the end of June. The same is true of the *monthly averages*. In 1951 and 1952 the maximum monthly averages were observed in September; in 1953 and 1954 in August (15% and 11% respectively), in 1955 and 1956 in October (8% and 18%), in 1957 in November (8%), in 1958 in September (12%); in 1959, with its abnormally warm spring, summer and autumn, the values were very low all through the year (less than 3%, in September only 1.6%). The shift in month of maximum values has proved to be related to a shift in the onset of winter in the Netherlands.

(4) In 1957 and 1958, 62% of the average asthma frequency values for the *boys'* residences was higher than that of the *girls'*.

(5) *Fog*, except perhaps in cities with much air pollution (which is extremely rare in the Netherlands), has no asthma-producing effect; The contrary is, rather, the fact, for periods of fog (characterized in the Netherlands by periods of little atmospheric turbulence and usually high barometric pressure) show very low asthma frequency. In February 1959, with 19 days of fog (against 7 normally to be expected), the monthly percentage of asthma frequency was less than 2%.

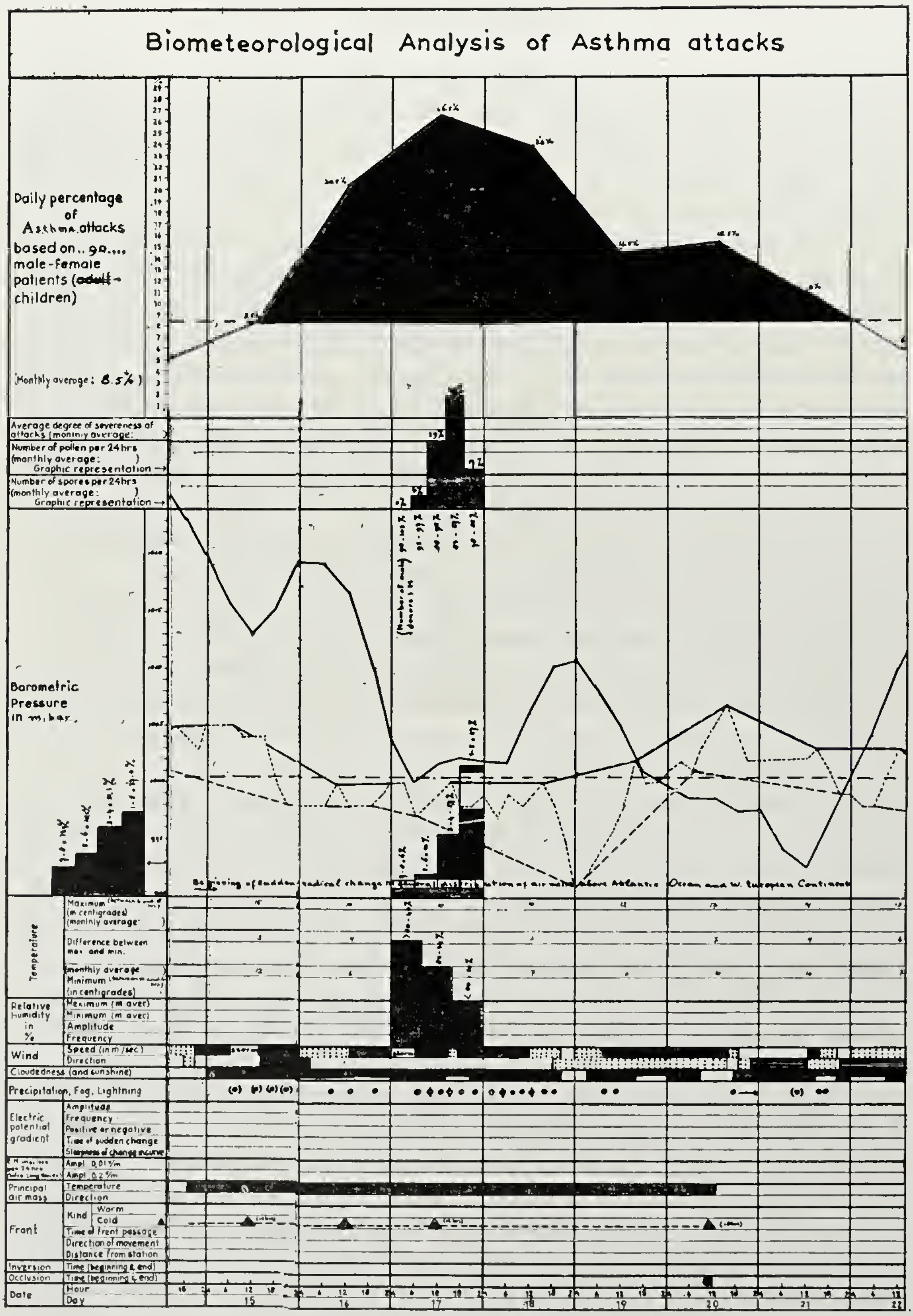


Fig. 84.

Steep rise of the daily percentage of asthma attacks in a group of 90 children at Hilversum (The Netherlands), during October 1955, after a period of quiet atmospheric conditions with a high pressure area over W. Europe (from 9–14 October 1955). The rise begins after the first group of a series of cold fronts, with rain and hail, reached the coast of W. Europe (for further details see ref. [1918a]).

(6) No direct relationship was found between days, months or years with very high *pollen or spore content of the air* and asthma frequency. In fact, periods of very high asthma frequencies are observed in late autumn, during which hardly any pollen or spores were found in the atmosphere. In some of the cases a correlation seems to exist, but a careful analysis shows that this correlation is not a causal one but is entirely due to the observed correlation between temperature, humidity, hours of sunshine, air turbulence and the number of pollen and spores in the air.

(7) A highly significant *statistical relationship* was found *between asthma frequency* and *certain phases in the weather:*

(*i*) In order to study the significance of the observed relationship between active cold fronts (or influx of cold polar air) and rise in asthma frequency a statistical analysis was carried out using the Gauss Integral of Probability (see p. 175). Using this Gauss method, it was found in 1956, for example,—a year of high asthma incidence in the Netherlands—that I.P. = 3.22. As I.P. = 2.33 is already significant at the 1% level (see p. 176), the observed correlation proves to be highly significant. It is even more so if holiday periods (with less trustworthy asthma percentages because of the small number of children and the greater influence of psychosomatic factors on children who are not permitted to go home) are eliminated. In this case the statistical significance is very much greater. Nor should we disregard the fact that asthma frequency may cease to increase when a third front follows upon two previous ones in quick succession. As in most physiological processes, over-stimulation may even have the reverse effect (see p. 199). If this fact is taken into consideration and only the first front passage is considered, we may speak of an almost perfect correlation between active cold fronts and the increase of asthma in the Netherlands.

In any statistical analysis of this kind the following considerations are likewise important: (α) From a physiological point of view it is very unlikely that an excess in asthma attacks would be observed exactly at the time of the passage of the cold front. As in most physiological processes, there will be a "time lag". Therefore, one should take as a criterion an increase within 24 hours after the passage of the front or after any other meteorological event. (β) As only a certain number of patients in a reservoir of people are in a condition to develop an asthma attack under specific weather stress, once all these people have an attack no further increase in the daily percentage of asthmatic patients in this constant reservoir of observed people can be expected. It is therefore not surprising that the daily percentages should cease to rise after a few days and may even decrease.

(*ii*) The asthma frequency increases rapidly after a sudden increase in general turbulence of the atmosphere if combined with the influx of cold air masses. The increase is most striking after a preceding quiet period. This change in turbulence is characterised by a sudden rise or fall in atmospheric pressure. Periods of steep barometric fall, due to rapidly approaching low pressure areas, have a particularly marked asthma-increasing effect if all these weather changes are accompanied by a sudden influx of cold polar or continental air masses followed by one or more active cold fronts (see Fig. 2 on p. 49 and Fig. 84 on p. 468). The latter are usually accompanied by great speed of movement, sudden change in atmospheric pressure and temperature after the passage of the front, heavy precipitation (rain, snow or hail), considerable disturbances in the electric field of the atmosphere (fluctuations of the electric potential gradient between high positive and high negative values), sudden changes in direction and velocity of the wind and so forth. Owing to these specific weather conditions, the average daily temperature and the maximum temperature gradually drop, often below the monthly average. In some instances the actually observed drop in the average dry-bulb temperature is small; the kata-thermometer, however, indicates clearly a sharp increase in the cooling effect of the atmosphere due to the increase in general turbulence.

(*iii*) During periods of slight atmospheric turbulence (usually coinciding in the Netherlands with a high pressure area in W. Europe, or with the influx of warm tropical air masses and active warm fronts), a sharp decrease in asthma frequency is observed.

(*iv*) The rapid succession of periods of cold and warm air masses, or cold and warm fronts, may create sinusoidal waves of periods with increasing and decreasing asthma frequency, but each with a relatively small maximum amplitude. If the succession is too rapid (*e.g.* within a few hours), often no effect at all is observed.

(*v*) If a sudden change in weather occurs, because a rapidly approaching deep low pressure area with warm tropical air is filling up with cold polar air, accompanied by decrease in general atmospheric turbulence, the asthma frequency increase but the amplitude remains small.

(*vi*) The same weather phase with cold air influx causes a considerably smaller increase in asthma frequency in winter than in summer.

(*vii*) A gradual fall in temperature, *e.g.* during a quiet cloudless night, or extending over several days without any appreciable turbulence, does not usually affect the asthma frequency.

(*viii*) In a healthy population group a general increase in diastolic pressure and haemoglobin content of the blood and low blood sedimentation rates are usually observed during or after periods of weather conditions creating an increase in asthma (see p. 318).

(*ix*) Broadly speaking, the sharp increase in asthma during approaching cold fronts starts at different times in boys and girls.

Possible causes of the observed weather–asthma relationships

Although the available data are not yet sufficiently comprehensive to provide a satisfactory physiological explanation for all the observed weather–asthma relationships, a number of well-established physiological facts may help us to understand the observed phenomena.

The various weather–asthma relationships suggest that severe dyspnoea is caused in asthma patients in the Netherlands predominantly by a sudden drop in environmental temperature combined with marked cooling effects resulting from considerable atmospheric turbulence. On the other hand, we have seen that during the cold months of January and February the average incidence of asthma is low and that, even when on certain days there is a noticeable increase in the incidence of asthma compared to the monthly average, this increase has far less amplitude than in summer or autumn. These two, apparently contradictory, phenomena suggest that at least two biometeorological processes in relation to asthma have to be distinguished, *i.e.*, (*i*) A general increase in physiological susceptibility to meteorological factors in relation to asthma from winter and early spring to summer and autumn, and (*ii*) superimposed on this pseudo–seasonal rhythm, short-term fluctuations in meteorological factors triggering off asthma. The former factor may be related to a number of well-established seasonal rhythms of a group of physiological and physico-chemical processes in the human body which may affect asthma patients in a heightened degree.

General biometeorological and acclimatisation studies of healthy persons have shown the following important differences between summer and winter:

(1) *Change in composition and physico-chemical state of the blood.* The calcium, magnesium, iodine and phosphate content of the serum is lower in winter; the haemoglobin content of the blood, in other words its oxygen-carrying capacity, is higher in winter than in summer, which is very important because an analysis of haemoglobin values of asthmatic children has shown that asthmatics have haemoglobin values of the blood considerably higher than normal subjects (see p. 315). The total protein and albumin content of the serum in normal subjects is also higher in winter than in summer. The globulins, particularly γ-globulins, are higher in summer.

(2) *Change in dominating activity of the different parts of the autonomic nervous system.* Diastolic blood pressure is highest in winter. This is probably at least partly due to increased activity of the orthosympathetic system during winter (or relative decrease in activity of the parasympathetic nervous system).

(3) *Changes in endocrinal functions.*

Cold stress and shortage of ultraviolet light in winter cause a decrease in the production of gonadotrophic hormones (sharply increasing in spring) by the anterior lobe of the pituitary, increased thyrotrophin and adrenotrophin production followed by hyperthyroidism (with intense congestion of the intra-alveolar capillaries and disappearance of the colloid from the alveoli), hyperparathyroidism, greater activity of the adrenal gland and of the liver (see pp. 279 and 287). The hypertrophy of the thyroid leads to increased metabolism and oxygen requirements. The increased adrenal function causes increased secretion of 17-ketosteroids (which are known to have a tranquillising effect on asthmatics) and increased capillary resistance (decreased permeability) of the membranes (see pp. 280 and 335).

(4) *Changes in sensitivity to thermal stress after acclimatisation.* Acclimatisation to cold stress during summer has proved to be more difficult than in winter; also, increased thyroid activity and metabolism after sudden cold stress are less in winter than in summer, owing to the continuous cold stress in winter. A long warm period leads to thyroid inactivity and therefore a sudden influx of cold air in such a warm period affects thyroid activity (and metabolism) more seriously than in a cold period. Recent experiments by Davis and Joy in the U.S.A. indicate that nude subjects exposed to 12–14° C for 2 hours showed in winter 90% less shivering than in summer, oxygen consumption being 50% less in winter as a result of the gradual cold acclimatisation during the winter months. Moreover, during spring and summer, with their increased ultraviolet radiation, more *histamines* are formed in the skin. During the same period the average 17-ketosteroid level of the blood is also lower (see below). All these, and probably several other, factors make the summer–autumn period a particularly favourable period for dyspnoea in persons (like asthmatics) with a generally overstimulated parasympathetic system (or understimulated orthosympathetic system).

Sudden cold stress, either during summer or winter, may start off the following physiological events:

(1) Abrupt *increase in thyroid activity, metabolism and oxygen requirements,* which may lead to increased pulmonary ventilation and alkalaemia. Studies of healthy persons at Leyden revealed a regular decrease in acidity of urine during influxes of cold polar air and the passage of active cold fronts. Studies by Seltzer (see p. 300) have shown that the oxygen requirements may differ considerably, depending on the body build and general typology of the person.

(2) Straube, Kalkbrenner, Scholz and Becker were able to show in 1950 (see p. 195) that the parasympathetic (acetyl choline) reaction always starts *several hours earlier* than the orthosympathetic (adrenalin) during the

passage of fronts. Both processes (increased thyroid activity and parasympathetic stimulation) may be responsible, at least partly, for a reflex stimulation of the constrictor fibres of the smooth muscles of the bronchi, causing dyspnoea. This may be especially the case in summer and autumn, before the subject is properly acclimatised to cold stress.

(3) Cold stress causes a sudden *increase in production of 17-ketosteroids* and other adrenal hormones, according to Zimmermann (see p. 516) increasing the general resistance to infection. The fact that in the biometeorological charts a rise in asthma frequency usually coincides with a rise in 17-ketosteroid production could be explained as follows: The cold stress period is generally preceded by warmer weather with low 17-ketosteroid levels and, therefore, less resistance to parasympathetic contraction of the bronchi. A sudden cold stress, affecting oxygen consumption and stimulating the autonomic nervous system, causes dyspnoea. However, it also increases 17-ketosteroid production which, after a few days, reaches a point where the bronchi are immune to this cold stress.

(4) As explained on p. 276, sudden cold stress lowers the *magnesium level* and may contribute to the muscular spasms of the lungs (see p. 465).

(5) Cold stress reduces the *capillary permeability* (see pp. 280 and 335) and hampers the oxygen intake and CO_2 release of the lung membranes.

(6) The great sensitivity of asthmatics to cooling effects also suggests that the *thermoregulation mechanism* in asthmatics is *less efficient* than in normal persons and, therefore, dysfunction of various hypothalamically controlled mechanisms in the body will occur sooner during weather stress.

A considerable amount of research is nevertheless still required to confirm these and previously mentioned hypotheses on the physiology of the weather–asthma relationship.

Possible microclimatic relationships between bronchial asthma and soil

Studies by Storm van Leeuwen *et al.*[1915] in Holland indicate that dry sandy soils are better for asthmatics than humid soils like heavy clay and peat. They assumed that more allergens are likely to occur in humid soils.

A similar but more extensive study was carried out by Tiefensee[1917] in East Prussia in 1926, an area almost entirely covered by glacial deposits. Of 1137 asthmatic cases 46% lived on basal moraines, 41% on initial glacial stream valleys, only 7% on the terminal push moraines, 4% on lateral moraines and 2% on sandy outwash plains, whereas the population density of the total population in these different areas was the same. The areas with high asthma frequencies are composed of humid clay and marl soils which are often flooded, whereas the soils of the lateral moraines are more sandy and better drained. The areas with low asthma incidence are topographically higher and more forested. Tiefensee also attributed this peculiar geographical distribution to differences in allergen distribution.

Since 1958 Varekamp and Voorhorst have studied in Leyden (Holland) the possible relationship between very humid old houses, with floors having a high percentage of wood-rot, and more modern, dry, houses with little wood-rot. Due to the high groundwater level in the Netherlands, 70% of the houses built before 1918 suffer from rot, against 11% in houses built after 1918. The degree of wood-rot was determined by the Wood Research Institute of the National Research Council. It was found that a significant statistical relationship exists between houses with a high percentage of wood-rot in the floors, and atopic asthma patients, with positive skin tests for house-dust allergens. This relationship was not evident in the non-atopic patients. For all that, skin tests with extracts of the floor-moulds did not support the allergenic theory. It is an interesting fact that the same statistical correlation was found between houses with a high percentage of wood-rot and rheumatoid arthritis (see later p. 550).

Harsh[1885] noted considerable differences in the geographical distribution of asthma on the W.coast of the U.S.A. For example, patients living near San Francisco Bay suffer from asthma but find relief a few miles inland. Harsh accounts for this by a difference in humidity. In other parts of the U.S.A. as well he observed that a higher incidence of asthma often obtains in areas of prevailing high humidity. He thought that humidity may make the house-dust more allergenic by favouring the action of micro-organisms on certain constituents of the dust; but a careful analysis of the microclimate of these humid asthma areas showed that in San Francisco Bay, for instance, the many foggy days and considerable cooling effects observed are more deleterious than the humidity as such.

Maunsell[1896] observed in London that 17 out of 19 bronchial asthmatics lived in houses within 180 yards of a waterway, or in humid basements, or in low-lying houses above hidden tributaries of the Thames; in other words, above a very humid subsoil.

The various observations described above seem to suggest that it is not differences in allergens that are responsible for the observed differences in the incidence of asthma; the cause would appear rather to be traceable to differences in microclimate, although in certain instances the house-dust itself may be responsible.

As explained on p. 225, the rate of cooling of the human body in humid houses in countries with considerable air turbulence, such as the Netherlands or England, is considerably greater than in the more modern dry houses. E. Prussia, in the areas where the incidence of asthma is low, and the sandy areas of Holland, are usually well wooded; therefore, in these wind-protected regions, there is little turbulence of the air. The soils are well drained and not humid as a rule. In other words, the rate of daily cooling is low. Hence, in view of the observations mentioned on p. 469, the soil-asthma relationship would appear less likely to be directly causal in association with differences in allergens (although in certain instances this may be so) than an effect of differences in local cooling of the body of the asthmatic patient with a poor thermoregulation system.

Another interesting aspect of the possible influence of specific micro-climates on bronchial asthma is the supposed improvement experienced by many asthmatics in *limestone or marly limestone caves*. If these observations could be confirmed, various explanations would have to be considered: lack of air turbulence, with fair constancy of temperature and humidity, probably lack of allergens, higher CO_2 content of the air (experiments by Tiefensee in 1929 suggest that asthma patients obtain relief from inhaling air rich in CO_2), change in ion content of the air (see p. 611).

Influence of high altitude

Almost all physicians who have seen asthma attacks diminishing in patients taken from low-lying country to high altitudes in the mountains, agree that the improvement is quite striking. It may continue for several weeks, even after the patient has returned to the lowland area. The first medical practitioner to adopt this measure was Denz who, in 1877, treated 6 patients at Churwalden (1214 m) in Switzerland. The same results have been obtained in recent years by raising the patient artifically to a high-altitude by means of a low-pressure chamber (see p. 638).

Although many clinicans are inclined to explain the improvements in mountainous areas in terms of the lack of air pollution and allergens and also of possible psychosomatic factors, the many established high-altitude physiological phenomena (see pp. 293 and 298) seem to indicate that the increased pulmonary ventilation, vital capacity, blood circulation in lung capillaries, adrenalin secretion, 17-ketosteroid secretion, etc.* in a patient taken to a high altitude, are the main causes of improvements apart from other favourable factors of *mountain climate* (see p. 27).

In view of these various observations a climatic treatment of asthmatics is to be highly recommended. High-altitude treatment in a low-pressure

* It is not excluded that the decrease in eosinophil leucocytes at high altitude (see p. 294), lowers the histamine content of the blood (see p. 194) and therefore diminishes bronchial spasms.

chamber, during which the patient is taken rapidly to a great altitude, combined with aerosol treatment (*e.g.* acid aerosols, rich in magnesium salts), ultraviolet radiation treatment and cold adaptation treatments (particularly during summer) have favourable effects which seem to continue for weeks and even for months.

Many other biometeorological aspects of bronchial asthma have been reported, but space prevents me from discussing this problem in more detail. Readers are referred to the refs.[1863–1922].

The meteorotropism of bronchial asthma has been discussed rather extensively, as compared to other biometeorological phenomena, because it is probably one of the most carefully studied biometeorological diseases and the methods discussed are applicable to many other related biometeorological problems.

Subsect. B. CANCER[2178–2285]

The possible influence of the meteorological environment on the origin, incidence and geographical distribution of cancer has hardly been studied at all, except for cancer of the lung and cancer of the skin. A more general study of the possible effect of meteorological environment on cancer would therefore seem to be warranted.

1. *Cancer — General*

If we assume that biometeorological factors play any part at all in the development of cancer generally, two possible mechanisms suggest themselves, *viz.*,

(1) *Direct effect* of one or more meteorological factors on the human body: (*i*) Through direct stimulation of certain organs causing a cancerous cell growth (cancer of the skin being a good example) and (*ii*) Through indirect stimulation of certain important physiological processes (endocrinal and hormonal more specifically), the influence of which on carcinomatous developments are known from various clinical studies.

(2) *Indirect effect* on carcinogenic substances in the atmospheric environment, which reach the body either through the skin or through body cavities, the lungs in particular.

The meteorotropic aspects of lung and skin cancers will be discussed in two separate sections, the latter by Dr. and Mrs. Mackie of Australia. The present section will deal with the possible effect on physiological processes, important from the point of view of the development of cancer. A meteorotropic mechanism of this kind would seem plausible for two reasons:

(1) It is known that a serious *dysfunction of the endocrinal system,* especially of the pituitary and adrenal glands, may play an important part in the development or acceleration of carcinomatous cell growth in various organs. For example, it has been reported by a number of research workers that in hypophysectomized rats both spontaneous and artifically created tumours (*e.g.* as a result of methylcholanthrene treatments) are extremely rare. On the other hand, large concentrations of various growth-stimulating hormones injected in animals seem to be able to produce artifical tumours; *e.g.*, thyroid tumours by thyrotropin, adrenal tumours by adrenocorticotropin, testis tumours by gonadotropin, etc.

In previous sections examples have been given of dysfunctions of the pituitary, thyroid and adrenal glands as a result of extreme weather or climatic conditions.

(2) Several observations, summarised by Tromp* in 1955, suggest the *significance of stress conditions* acting on the development of cancer.

G. Donagh reported in 1950 on the retarding effect of psychologically favourable conditions on the development of metastases from malignant tumours in cancer patients. Such favourable conditions were observed after changes in the climatic environment of the patient, thermal baths, etc. Some mental stress conditions accelerated the growth of tumours.

Studies in the U.S.S.R. by Raushenbakh, Zharova and Rhokiova (in 1952) and by Kozhevnikova (in 1953) (see ref. in footnote) indicated that there is a considerably higher incidence of tumour development (after treatment with methylcholanthrene) in mice made neurotic by regular exposure to electric or acoustic stimuli than in a non-stimulated control group. Similar results were obtained by Rashkis (in 1952) in the U.S.A. if the stress was created by forcing the mice to swim.

Studies in the U.S.A. by Abrams, Bacon, Blumberg, Gengerelli, Leshan, Shands, Stephenson, Tarlau, West and others on the statistical relationship between certain types of cancer and psychosomatic factors (personality patterns of patients, etc.) strongly support the view that stress conditions usually accelerate the development of carcinoma (see ref. in footnote).

The influence of the environment on mammary carcinoma in rats was demonstrated by Andervont in 1944 and by Mühlbock in 1950. It was found that of 50 female mice of the same pure genetic strain 29% developed mammary carcinoma in the experiments if all animals were placed in the same zinc cage, whereas this percentage increased to 56% if the 50 mice were split into 10 groups of 5 mice and to 83% if each animal was isolated. It is

* Note by S. W. Tromp: Psychosomatische Faktoren und der Krebs (insbesonders der Lunge und der Mamma), *Der Medizinische*, *13*, 443–447, 26 March (1955).

not yet known whether the decrease in density and, therefore, the greater motility of the animals, the difference in body temperature of the mice or a difference in psychological factors was responsible for this environmental effect.

Considering the fact that similar physiological and hormonal processes occur during these various stress conditions similar to those observed during climatic stress, there is some ground for assuming that certain climates with extreme temperature, humidity and air turbulence conditions could likewise affect the development and incidence of carcinoma in different parts of the world.

It is also known that one of the factors affecting the formation of metastases is the cohesion of the cells. Coman stated in 1954 that cancer cells appear typically to cohere less than normal tissue, due, at least partly, to the relatively low calcium content of cancer tissue, to other physico-chemical properties of the blood and of other fluids surrounding the tissue cells. As both the calcium level and other physico-chemical properties of the blood can be affected by the weather and climate (see p. 276), the process of metastasis may also conceivably be affected by extreme climatic conditions.

Another interesting biometeorological problem is the possible effect of high altitude on cancer. Experiments by Warburg in 1926, repeated by Campbell in 1931, suggest that tumour growth in cancerous rats is inhibited if the animals are exposed to laboratory conditions comparable with very high altitudes (17,000–40,000 ft.). The tumours have a tendency to become necrotic.

Later studies by Sundstroem and Michaels in 1942 tend to confirm these observations[2197]. The regression of tumours, however, was observed only when the total air pressure was reduced; regression failed if the oxygen tension only was diminished. According to Sundstroem, the average regressional rate after 17 days' exposure to 360 mm pressure was 39%, and 45% under 300 mm pressure. The regressing tumours began to grow again when the tumour-bearing rats were adrenalectomized and given just enough cortical hormone to keep them alive. As the total number of mice used in these experiments was small, the experiments will have to be repeated on larger groups of animals.

So far, the mechanisms involved are unknown, but in view of the effect of low pressure on various physiological processes (see pp. 293 and 298), it seems possible that changes in hormonal production are involved in this high altitude effect, especially changes in activity of the adrenal gland.

2. *Cancer of the Lung*

Recent studies by Lawther [2335, 2336], Stocks [2212, 2213], Tromp [2214], Waller [2215] and others suggest that air pollution may be one of the possible aetiological factors of lung cancer. The following observations seem to support this view point.

(1) *The excess mortality from lung cancer in urban, industrialized, areas as compared with rural districts.* In England and Wales in rural districts the standardized mortality rate for cancer of the lung in the male population (period 1950-1953) was 64, in urban areas under 50,000 inhabitants: 84, in areas with 50,000 - 100,000 inhabitants: 93, in urban areas over 100,000 inhabitants: 112. The same is true for the female population. Similar relationships were found by Tromp in the Netherlands in 1955 and by Kreyberg in Norway in 1956. However, in Holland and Norway the high urban/rural ratio occurs despite the fact that in towns the air pollution is very slight. This argument cannot, therefore, be accepted merely at its face value.

(2) *The clear relationship in England between lung cancer and population density.* Stocks and Campbell showed in 1955 that in England this correlation obtains at all levels of smoking among the population; in other words, the population density correlation is not only due to differences in smoking habits in areas with different population densities.

(3) *The close correlation between the incidence of lung cancer and the degree of air pollution in the area* (studies by Stocks). In a recent study by this author[2213a] it was pointed out that a very significant statistical correlation was observed between *high smoke density* and *lung cancer* mortality in England. The relationship could be established in 26 areas of N. England and Wales, in 45 districts of Lancashire and the West Riding of Yorkshire and in 30 County boroughs. Similar, though weaker, correlations were found in Greater London. Also cancers of the *stomach* and *intestine* are significantly related with smoke in the County boroughs. Cancer of the *breast* in females does not show a relationship with smoke.

(4) Whereas the average lung cancer mortality in the coal mining districts in the Netherlands (see also Figs. 34 and 35 on p. 172), both for males and females, is lower than the average lung cancer mortality of the coal mining province of Limburg as a whole and even much lower than the whole country, *in the true mining centres,* with their large air-polluting chemical industries, *lung cancer mortality is greater than in the province as a whole* (studies by Tromp).

(5) The apparent *relationship between the combustion of fuel, and cancer,* as demonstrated by the high incidence of cancer of the scrotum in chimney

sweeps, the frequent occurrence of skin cancer among gas workers and the carcinogenic effect of painting the skin of animals with extracts of coal-tar.

Although some of the observed differences, *e.g.* between rural and industrial areas, may be due to other, unknown, sociological factors, the air pollution theory is supported by the discovery of carcinogenic substances in the air in various heavily polluted areas. The carcinogenic properties of 3,4-benzpyrene — which was isolated in 1930 by Sir Ernest Kennaway and co-workers — were described on p. 97. Kennaway *et al.* had evidence that it may be produced by pyrolysis (*i.e.* decomposition at high temperatures in the absence of oxygen) of many organic substances. The distribution in the air was studied by Kennaway, Commins [160], Kotin[2207], Lawther[2235], Waller[2215] and others. For this purpose 82 cm^3 of air were filtered through a drechsel bottle containing pure liquid paraffin for 38 days. In this solvent 3,4-benzpyrene fluoresces very strongly, the liquid paraffin not being fluorescent. Recent studies in Paris confirmed the findings of British and American research workers. Extracts from air samples in Paris produce lung cancer in rats.

Apart from 3,4-benzpyrene, other carcinogenic substances are found in town air: 1,2-benzanthracene, 1,12-benzperylene, benzene, chrysene, epoxides, arsenic, etc. (see ref.[2206a]).

Recent studies by Stocks (in 1960) in 23 localities in England, using spectrographic air analysis for 13 trace elements, showed a significant correlation between lung cancer and the beryllium and molybdenum content of the air. Weaker associations were found for arsenic, zinc and vanadium. In males, beryllium, molybdenum and vanadium showed also associations with other types of cancer. Cancer of the breast did not show relations with any of the 13 trace elements.

Despite the fact that considerable evidence supports the view that air pollution may be a causative factor in the development of lung cancer, various recent studies, particularly by Lawther, suggest that although it may play some part in the causation of lung cancer, it is probably not responsible for the spectacular rise in the incidence of the disease during the last 20 years.

In the following section Dr. and Mrs. Mackie (Australia) will discuss the direct effect of solar radiation in inducing cancer of the skin. It is chiefly in the U.S.A. and Australia that this matter has been studied. Apparently, the nearer to the Equator the white population lives, the greater is the incidence of cancer.

In 1947, in the Northern part of the U.S.A., the incidence rate for skin cancer in the white male population amounted to 33.4/100,000 inhabitants (4.3 in the non-white population), in the Southern States 143.3 (5.4 in the non-white population). According to Macfarlane *(verbal information)*, in 1960 the incidence on the coast of Queensland (Australia) was 11,000 cases per million of the male population, females having about half that skin cancer rate. Further inland the male incidence is estimated to be even 15,000 per million. Macfarlane pointed out, rightly, that customs that have grown up in the last 20 or 30 years, such as working in shorts in the tropics, excessive sun-bathing and so forth may have serious consequences for the white population in tropical countries.

3. Cancer of the Skin

by

B. S. MACKIE and LEILA E. MACKIE*

Introduction

The subject of this section provides a most interesting aspect of the study of man in relation to his environment. Its complete coverage requires investigation of certain racial, geographical and climatological factors as well as a study of the biology of skin cancer itself. With a suitable climate and a susceptible race, skin cancer becomes a major medical and social problem. For example, in Australia, the country with the highest incidence per head of population[2221-2224], skin cancer provides more than half of all diagnosed cancers[2224].

The outstanding feature of skin cancer is that it occurs almost solely *on areas of the body exposed to the elements* (types of cancer which occur with equal frequency on exposed and covered areas are uncommon, comprising lesions such as those caused by arsenic and ionising radiations, and they will not be considered here). This fact of extreme predilection for exposed skin is highly significant as it is strongly indicative of an external causative factor. Its truth is readily established by examination of patients in a major clinic[2236, 2239, 2242, 2247, 2254b,c, 2262a, 2267-2269, 2273, 2283, 2284], and it is embellished by the added observation that cancers are seen more often *on the surfaces of exposed parts* which receive more solar radiation.

The next important point is the variability in resistance of different subjects. Again, clinical examination is the key and the observation is that skin cancer develops readily in fair skin, but less readily in proportion to the

* We are indebted to Mr Rolf Bradley for the photographic reproductions and the diagrams used in this section.

depth of natural skin pigmentation[2222, 2223, 2239, 2242, 2246, 2254b, c, 2262a, 2269, 2273, 2284].

The immunity thus conferred by melanin, the pigment of the skin, depends upon *heredity and race*. In Fig. 90 (p. 488) it is seen that humans can be divided into three main types, with endless intermediate grades, according to their degree of pigmentation. Type 1 has little or none, Type 2 has well-developed basal layer pigment and Type 3 has ample pigment in all epidermal layers. Cancer is seen mainly in those fairer than Type 2 while races with browner complexions are seldom affected[2216, 2220, 2232, 2236, 2248, 2250, 2250a, 2280].

These data of predominant occurrence on exposed parts in inverse proportion to the depth of pigmentation suggest that solar radiation is causally involved.

A number of other observations confirm this premise. Experiments with animals have shown that sunlight readily *produces skin cancer in albinos* and that the most active wavelengths lie in the ultraviolet range between 2900 and 3200 Å [2226–2230, 2241, 2277, 2278]. The same range is probably active in humans as well, since the incidence of skin cancer is much greater in regions closer to the equator when similar population groups are considered. This latitude effect has been observed by several workers in the U.S.A. and Australia[2181, 2224, 2225, 2233, 2254a, 2261] and is presumed to depend on the increased proportion of ultraviolet light (UVL) which penetrates the earth's atmosphere when the sun approaches the vertical. Atmospheric absorption of more horizontal rays may depend on ozone[2266]. Daylight and sunshine hours are bound up with latitude and do not play an independent role as they generally parallel the nearness of the sun to the perpendicular. Belisario has discussed their effect[2224].

Possible influences from rainfall, clouds, humidity, temperature and winds are difficult to assess. There is no evidence that they have any direct bearing on the occurrence of cancer, although it is probable that they qualify the extent of solar exposure. For example, pleasant conditions encourage the discarding of clothes and the disuse of weather protectors. On the other hand, excessively high temperatures and humidity discourage open air activities as also do cold, rain and wind.

High standards of living with ample outdoor space and diverting geographical features such as lakes and beaches all increase exposure and resultant cancers. Rural and seaside occupations act in the same way. Thus *both sportsmen and outside workers are more commonly affected* than those who spend less time in the sun[2189, 2254b, 2274, 2284].

Altitude would be expected to aid cancer production because the intensity of UVL increases with elevation and these wavelengths are well reflected by snow[2259]. There are no statistics however to support this view.

Finally it is apparent that other stimuli to epidermal growth such as trauma, local inflammation and chemical carcinogens are more likely to precipitate cancer in skin which has suffered repeated solar exposure. Interesting examples are flax workers cancer of the lower lip and hands[2253]. Belisario's traumatic cases[2224] and Ward's fishermen who handled tar-covered nets[2284].

The effects of sunlight on the skin

Sunlight, covering a wide range of wavelengths, has a number of different effects on the skin (see pp. 339 and 343). The infa-red fraction causes an immediate erythema and also aids pigment production. Visible light gives little demonstrable reaction. As stated above, the important rays from our point of view appear to be UVL although one cannot discount a possible contributing influence from the longer wavelengths.

UVL is necessary for the activation of vitamin D in the outer layers of the skin and it also causes increased pigmentation by a mechanism as yet unknown (see p. 340). Its other physiological effects are the production of a delayed erythema (true sunburn) and the appearance several days later of an increase in thickness of the stratum corneum (cornification). In the case of a single exposure this thickening simply peels off but on regularly exposed areas there develops a permanently thickened stratum corneum[2227, 2229, 2230, 2263]. It is important to note that both cornification and the tendency to sunburn are more marked in Type 1 than in Type 2 or Type 3 subjects[2227, 2229, 2230, 2263].

Pathological reactions to UVL consist of degenerative changes and skin cancer. For their production repeated exposure to the sun over a period of years is necessary, the time interval being longer in proportion to the degree of skin pigmentation.

The degenerative change known as *senile elastosis* or *collagen degeneration*[2263] can be seen even in adolescents if they are of Type 1. Clinically it appears as a minute yellowish mottling of the exposed skin, mingled with irregular pigmentation and redness. Later the skin creases become accentuated and the skin looks thicker although it feels thinner. Microscopically there is progressive degeneration of the connnective tissue in the upper corium. It is usually on this background that solar pre-cancer and cancer occur.

The *pre-cancerous changes* are solar keratosis (including cutaneous horn), keratoacanthoma and lentigo.

Fig. 85.
Solar keratosis on the lower lip of a woman aged 41. She wore lipstick only when in the city. Note the linear shape of the lesion along the portion of the lip most exposed to the sun.

(1) *Solar keratosis* (Figs. 85 and 87) is a very slowly growing, horny excrescence, varying from a granular roughness to a hard mass elevated even one centimetre above the surrounding skin. It always arises in the presence of well-developed collagen degeneration and it shows premalignant hypertrophy of the epidermis and a chronic dermal inflammation (Fig. 86).

(2) *Keratoacanthoma*[2276, 2285] is a very interesting lesion which resembles squamous cell carcinoma (see below) but it grows much more quickly, only to heal spontaneously in most cases.

(3) *Lentigo* is simply a brownish or black, irregularly shaped, flat spot which shows microscopically a marked increase of the pigment-forming cells in the epidermis.

True cancer consists of an uncontrolled multiplication and penetration into deeper tissues of cells normally found only within the epidermis. The three forms of cancer which may be caused by UVL are squamous cell carcinoma, malignant melanoblastoma and basal cell carcinoma.

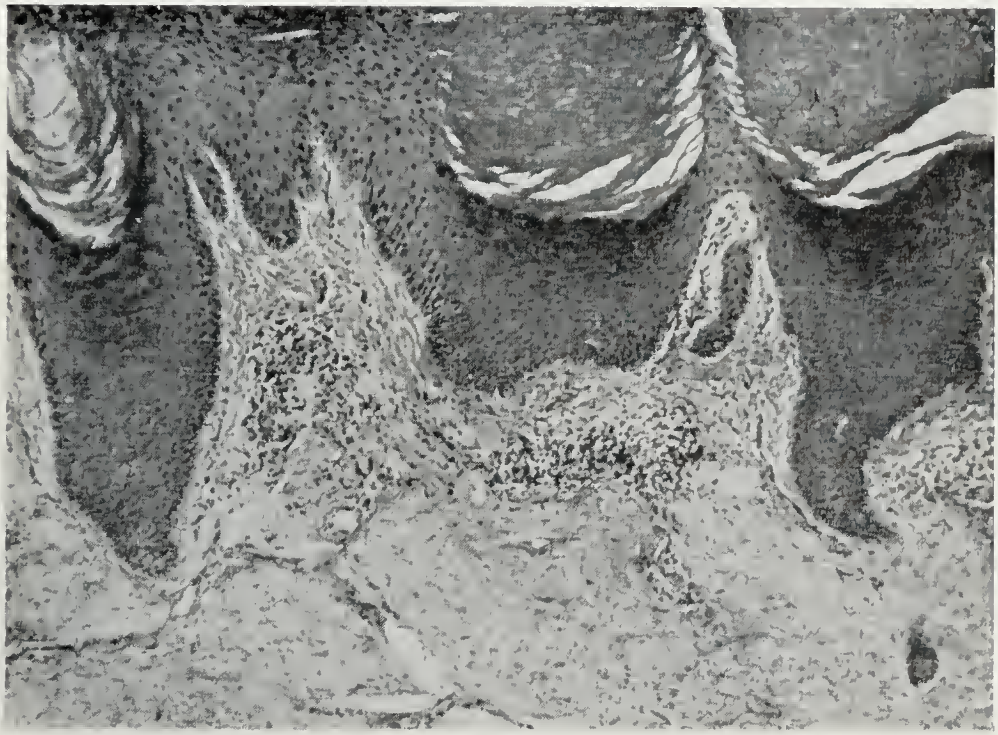


Fig. 86.
The histological picture of a typical solar keratosis, showing well developed collagen degeneration with an inflammatory reaction in the dermis and prominent hyperkeratosis and parakeratosis.

Fig. 87.
Squamous cell carcinoma and several solar keratoses on the forehead of a man aged 73.

Fig. 88.
Malignant melanoblastoma arising in a patch of lentigo in a woman aged 78.

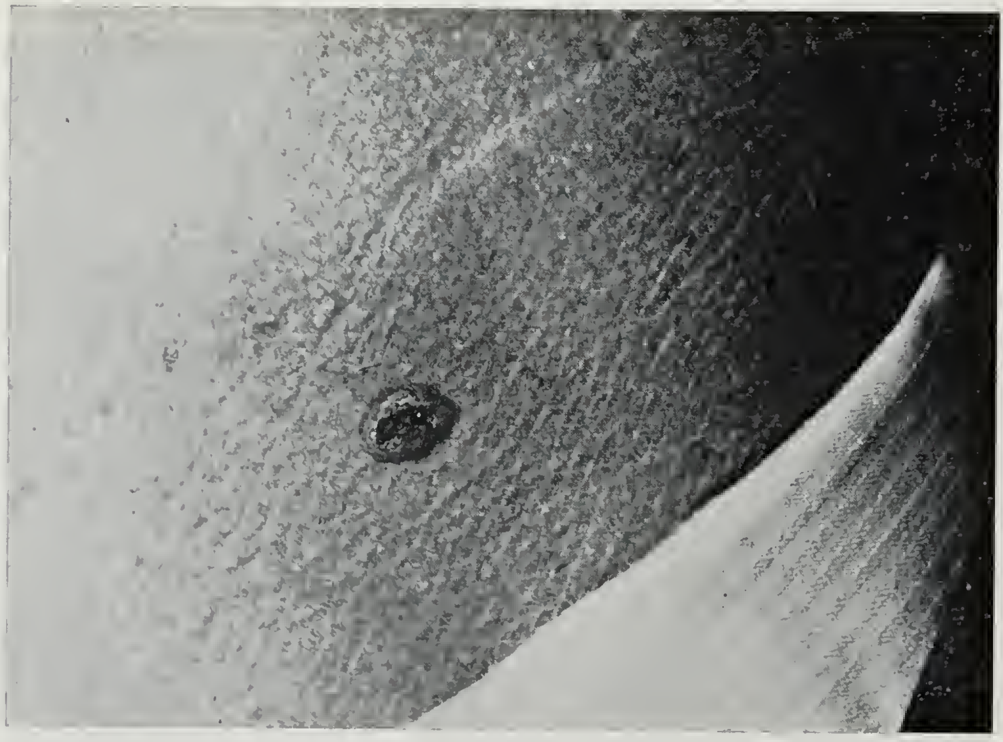


Fig. 89.
Basal cell carcinoma on the neck of a man aged 29.

(1) *Squamous cell carcinoma* (Fig. 87) develops usually from a pre-existing solar keratosis as a hard, pink to white, rounded, elevated lump either surmounted by adherent keratosis or showing an ulcer in the centre. Sooner or later the tumour cells metastasize to the regional lymph glands or spread by the blood stream and the patient's life is in jeopardy. The most malignant lesions are those found on the lower lip which also is affected more commonly than any other skin region of similar size.

(2) *Malignant melanoblastoma* is an uncommon but dangerous type of cancer, in the cause of which UVL appears to act as a contributing carcinogen[2192, 2200, 2234, 2251, 2254a, b, c, 2262]. In its less deadly form, known as Hutchinson's melanotic freckle (Fig. 88)[2219, 2252, 2262b], it arises as a black nodule in an area of lentigo, mostly in elderly people on the cheeks, and solar exposure appears to be the major causative factor.

(3) *Basal cell carcinoma* (Fig. 89) is the most common form of skin cancer. It is seen more on the face and neck than other exposed areas and usually appears first as a small pearly nodule which progresses slowly into a lump or an ulcer. Locally destructive, but rarely metastasizing, it is often known as rodent ulcer. Most lesions are solar in origin but some seem to have a naevoid basis as well.

The histology of these cutaneous malignancies[2257] is a picture of dermal and subcutaneous invasion by strands and groups of cells from the epidermis. The invading groups resemble prickle cells in squamous cell carcinoma, melanoblasts in malignant melanoblastoma and basal cells in basal cell carcinoma. Almost all cases show collagen degeneration[2262b, 2263] when of solar origin.

The mode of action of ultraviolet light

In view of the ease of study of ultraviolet carcinogenesis it is surprising that so little work is being done in this field. One would expect that increased investigation of the topic could produce results helpful in cancer study in general. Perhaps the relative simplicity of clinical application of different wave-lengths by a recently developed lamp will be beneficial.

UVL has the capacity of undergoing photobiological absorption when its energy is used to produce a biochemical change. It is assumed that cancer production depends in some way on this fact.

Unfortunately the study of the transmission and absorption of UVL in its passage through the skin is very difficult owing to the extreme scattering caused by the outer layers of the epidermis. It seems probable, however, that the gradient of absorption in regularly exposed skin of Type 1 and 2 is as shown in Fig. 91 (based on a number of papers[2217–2219, 2226–2230, 2237, 2251, 2255,

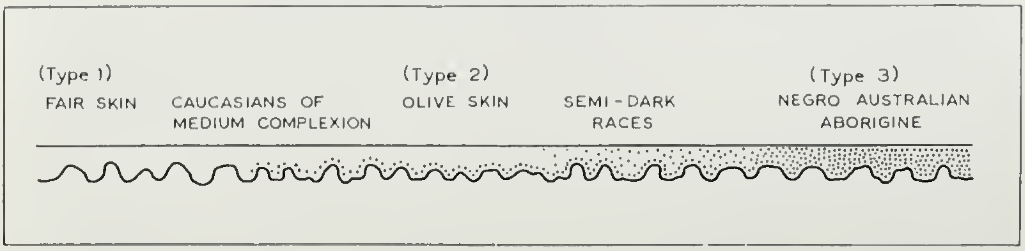


Fig. 90.
The skin pigmentary types and their reaction to sunlight. As the amount of pigment in the skin increases (→), the sensitivity to sunlight, as shown by redness and peeling, decreases (←) and the incidence of skin cancer and collagen degeneration decreases (←).

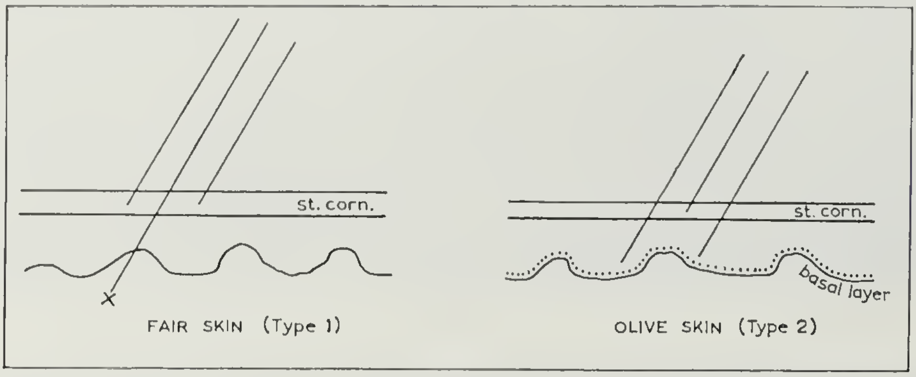


Fig. 91.
The relative absorption gradients of ultraviolet light in both fair and olive skins which have been regularly exposed to the sun. In fair skin the stratum corneum, being thicker, absorbs more ultraviolet light but the absence of a basal layer of pigment permits significant penetration to the dermis.

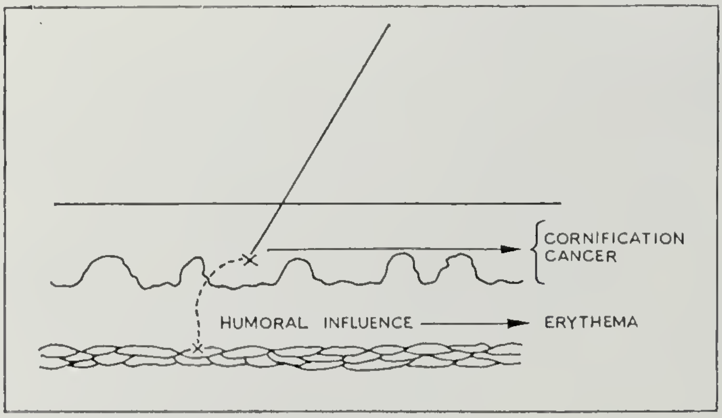


Fig. 92.
Blum's theory. According to this theory, cornification and cancer are the direct result of absorption of ultraviolet light in the epidermis while erythema is caused by permeation of a chemical from the site of absorption to the vascular plexus.

[2258, 2260, 2264]. It is seen that the thicker stratum corneum of Type 1 absorbs more than that of Type 2. However, the basal layer pigment of Type 2 prevents passage of rays into the dermis while in Type 1 a small percentage of the incident energy is absorbed in the connective tissue layer.

There is no proof yet of the site of effective absorption in carcinogenesis, the main theories being as follows:

Blum (see Fig. 92)[2226–2230] believes that carcinogenesis depends upon simple, long term absorption of UVL by the epidermal cells, while erythema is due to permeation of soluble products of photobiological change (humoral influence) from the epidermis to the blood vessels. The theory is based mainly on work similar to that of Miescher[2265] and Guillaume[2245].

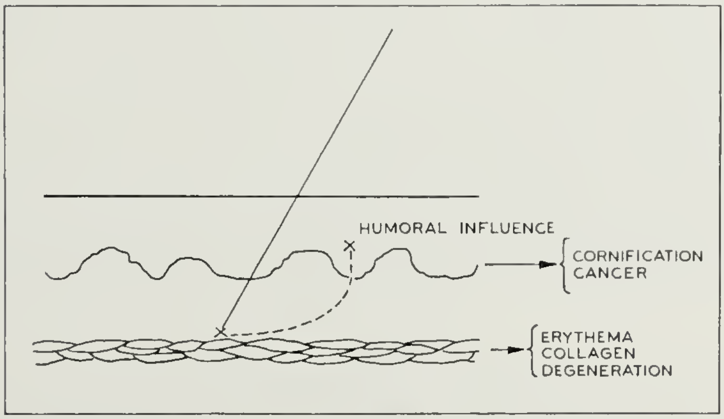


Fig. 93.
Mackie's theory. It is suggested that the absorption of ultraviolet light in the region of the vascular plexus causes erythema and later collagen degeneration by a direct effect, while a consequent alteration in the normal dermo-epidermal biochemical interchanges produces cornification and cancer.

The authors (see Fig. 93) suggest that absorption of UVL in the region of the superficial blood vessels produces erythema and, over a long term, collagen degeneration by a direct effect. At the same time, absorption in this site is thought to disturb the normal dermo-epidermal fluid-borne chemical interchanges so that a stimulus (humoral influence) is provided to epidermal cellular division, giving cornification in the short term and cancer over a period of years.

McGovern *(personal communication)* agrees with the authors on the site of effective absorption but considers that cancer is a result of poor epidermal nutrition caused by collagen degeneration.

Prevention and treatment

The prevention of skin cancer is of considerable importance in regions where populations of light complexion enjoy an equable climate with high ultraviolet exposure.

Education of the population in simple prophylactic measures should be observed. Hats, long-sleeved shirts, sunshades, such as beach umbrellas, and avoidance of unnecessary sunburning are the most effective means. Many people deliberately sunbake in the belief that a tanned skin is healthy and this myth requires public explosion.

Much attention has been given to the development of lipsticks, lotions and creams which absorb UVL and thereby reduce its penetration into the skin [2270, 2279]. These preparations are readily available and are definitely of value.

Other workers[2235, 2256, 2272, 2281, 2282] have studied internal medication designed to reduce the sensitivity of Type I individuals and enhance their pigmentary capacity but to date they offer no reliable benefits.

Active treatment consists of destroying each lesion by the method most suited to the type of growth, its site, size and stage of development and the patient's need for a healthy but unnoticeable scar. The destructive measures employed include radio-therapy, surgery, electro-desiccation, galvano-cautery and freezing by carbon dioxide snow or carbon dioxide–acetone slush.

Subsect. C. EYE DISEASES

Many publications have appeared on the possible relationship between weather, climate and eye diseases. Research workers in this field are recommended to study the original publications indicated in the references[2286–2327].

Of the various studies only two will be discussed in some detail, *viz.*, the effect of weather, climate and season on acute glaucoma and on retinal detachments.

1. Glaucoma (Acute)

Glaucoma is a dramatic eye disease, the aetiology of which is still unknown. It is characterized by excessive intraocular pressure, causing hardness of the eye and even blindness. It develops gradually or comes on suddenly (acute glaucoma), usually after the age of 50. It is more common among females than males, it occurs most frequently in the right eye and is particularly common in patients suffering from arteriosclerosis and members of Jewish race. The initial symptoms are slight headaches, pressure in the eye and reduced eyesight increasing to severe pain radiating from the eye to the upper jaws and head. The eyesight declines considerably at this stage and may eventually fail altogether. Several physicians at the beginning of this century noted a distinct relationship between weather and season and acute glaucoma. A brief summary of these studies seems appropriate:

Steindorff[2327] studied the clinical data of the Ophthalmic Clinic of Berlin for the period 1885–1902. During this period, 7181 patients were treated there and 83 of these (77 women) – 76 of whom were over 50 years of age – suffered 102 attacks of glaucoma, the exact day and hour of onset being known in only 68 of these 102. The distribution of these attacks over the various months of the year, expressed as a percentage of the total number of eye patients treated, is as follows: January 2.9%; February 1.8%; March–April approx. 1.4%; June 0%; July 0.7%; August 1.1%; September–October 1.5%; November–December about 2%. In other words, the *highest incidence* of acute glaucoma seems to occur *during the coldest months of the year.* If the average temperature on the days of attacks are compared with the average monthly temperature, it is found that the *glaucoma attack in winter occurred on very cold days and in summer on very hot days* (see pp. 507 and 508), Steindorff accounted for this relationship by changes in blood pressure due to extreme temperature conditions, which are particularly pronounced in older people whose thermoregulation system is poor (see p. 229) and who are suffering from advanced arteriosclerosis.

Studies by Schüssele in 1899 and extended by Bauer[2298] in 1903 confirmed Steindorff's observations. At the Ophthalmic clinic of Tübingen (Germany) 446 cases of acute glaucoma were analysed (279 women as against 167 men). Again a *maximum was found in January and a minimum in June.*

Maynard[2318] reported on a survey in an Ophthalmic clinic in Calcutta (India) for the period 1901–1906. The *maximum* number of patients appeared in *July* during the wet monsoon when the rainfall and number of sunless days reaches a maximum.

In Parma (Italy), between 1901 and 1920, 584 cases of glaucoma occurred, *i.e.* 1.65% of all observed eye diseases. According to Rebucci[2322], the *majority of cases was observed in the winter season.*

Margrit Rohner[2323] described 200 cases (122 females, 78 males) at the Ophthalmic clinic of Basle, observed during the period 1920–1926. The majority of the patients was over 50, more particularly within the age group of 65–79 (without correcting the age-group structure of the population, the maximum number of cases is found between the ages of 55 and 59). This Swiss material likewise indicates that the *highest acute glaucoma incidence* is in *winter* (October–February), *lowest in summer,* with the maximum in

November and the minimum in July–September (winter-summer ratio is about 9 to 1).

In 1932 Koike[2315] reported on the geographical distribution of glaucoma in Japan as observed in the Ophthalmic clinic at Osaka. The areas of Toyama, Kappazawa and particularly Nagano had very low glaucoma figures as compared with other areas in Japan. The former areas enjoy sunny pleasant weather conditions in contrast to other parts of Japan.

Studies made by Pillat[2320] at the University Ophthalmic clinic of Peking (China) in 1933 confirmed the findings of previous studies by Hopkins in 1892 that glaucoma is extremely rare among the Chinese (roughly 1.1%). The same seems to be true for the Japanese (according to Joshida, in 1927, only 0.86%). The average blood pressure of the Chinese is also low compared with that of Europeans (studies by Cruikshank in 1923 and Tung in 1930). Pillat observed *two seasonal maxima in China*. The incidence is highest in the winter months characterized by very cold continental winters and cold north winds. A second maximum occurs in May, despite the fact that this is a period when most of the population is working on the land and is therefore less inclined to visit clinics. During the first part of May there are many N.W. storms and influxes of polar and tropical air masses alternate. At the end of May the southern warm monsoon winds prevail. It is a well-known fact that Europeans in Peking often felt uncomfortable (insomnia, nervous tension) during the first part of May.

Fischer[2290] published in 1934 an interesting paper on interocular pressure and weather, studied in 710 patients (of whom 391 were males, 319 females) at the Ophthalmic Clinic of Leipzig (Germany) from 1927 to 1932. He was able to study daily changes in only 344 of these patients and could not, therefore, use the remainder as material for his work. The following results were obtained: (*i*) Extreme temperatures do not in themselves appear to affect the interocular pressure. If they did, both the Tropics and Arctic regions would have the highest incidence of glaucoma, which they have not; (*ii*) The author was unable to detect any relationship with the daily difference between maximum and minimum temperature; (*iii*) Pressure changes were greatest on days of extreme departures of average temperature from that of the preceding days; (*iv*) Of 43 cases of acute glaucoma 88% occurred on days when either cold or warm fronts were traversing the region. No relationship was found between attacks and the rate of barometric fall or rise. Similar reports were given by Mrs. Löffler in 1930, who studied abundant material in Vienna (verbal information published by De Rudder[6, p. 62]).

Interesting observations connected with the problems studied by Fischer at the Ophthalmic Clinic of Göttingen were published by Huerkamp[2310] in 1952. Ten thousand interocular pressure recordings were taken from 500 glaucoma patients. Between 3 and 6 the pressure is lower than at 8 and 17 hours. From 3 to 6 the pressure increases gradually by 8%. This observation suggests that the result of weather stress on acute glaucoma may depend also on the hour of the day (see p. 201).

Brückner[2302], using the material of the Ophthalmic Clinic of Basle (Switzerland), reported in 1938 and 1941 on the statistical relationship between acute glaucoma and passages of weather fronts. Sixty-six percent of all cases coincided with fronts.

Schorn[2326] studied 91 cases of acute glaucoma, observed during the decade of 1932–1942, in 76 patients at the Ophthalmic Clinic of Cologne (Germany), in order to test Brückner's observations. As in other studies (*e.g.* Brückner and Fischer), only those cases were used of which the exact time and day of attack were known. Using the statistical n-method (see p. 176), he found a 96% statistical significance. Later studies by Berg, who used ampler material, indicated an even higher statistical significance. Almost 80% of the glaucoma attacks occurred on the day of the passage of a weather front, or within the next 24 hours. They are particularly frequent on days when there is great atmospheric turbulence.

A more recent study carried out in 1955 by Sautter and Daubert[2324], using 64 cases of acute glaucoma at the Ophthalmic Clinic of Tübingen (Germany) during the period from January 1950 to November 1953, indicates statistically significant relationships between acute glaucoma and occlusions (see p. 19) or influx of cold air masses, in particular during periods of great atmospheric turbulence.

Similar studies were carried out by Kästner and Brezowsky[2300] at the Ophthalmic Clinic of Münich (Germany) from January 1953 to February 1958, covering 129 cases of acute glaucoma. Brezowsky used Ungeheuer's weather-phase method (described on pp. 24–25) for the biometeorological analysis. It was found that acute glaucoma occurs most frequently during weather phases 3, 4 and 5 (in particular during the influx of warm air masses); in other words, in the periods just before and during unpleasant weather changes. These correlations are mathematically significant.

We have discussed fairly extensively a great number of these carefully planned biometeorological glaucoma studies, as they furnish a good example of the many statistical meteoropathological studies carried out during the last 50 years. In virtually all cases satisfactory co-operation was secured between a well-known Ophthalmic clinic and a Meteorological institute.

Accurate clinical data only were used for these studies. The facts appear to have established beyond doubt that acute glaucoma is a typical meteorotropic disease and that the attacks are precipitated during periods of great atmospheric turbulence such as are apt to prevail during the passage of weather fronts. This seems to suggest that serious disturbances of the thermoregulation mechanism (working inefficiently in older people) may be one of the factors involved, which in turn could affect the autonomic nervous system and the changes in blood pressure.

On p. 574 Tromp will describe his observations at Leyden (Holland), where he found an increased percentage of relatively high (non-pathological) blood pressure values in a healthy group of the population in winter (particularly in February, the coldest month in Holland), this percentage decreasing again in summer. Sometimes a secondary peak may occur in spring (*e.g.* May), depending on the general weather conditions.

It is also an interesting fact that the yearly incidence curve of glaucoma is the same as the mortality curve of arteriosclerotic heart diseases in the Netherlands (see p. 508), revealing a close association with the average monthly temperatures.

Whether the usually higher tonus of the orthosympathetic nervous system in winter, in regions outside the polar circle where people are not completely adapted to cold, has anything to do with the seasonal incidence of acute glaucoma is a question that will have to be studied in the future together with other meteoro-physiological aspects of acute glaucoma.

2. *Retinal Detachments*

Retinal detachments are particularly common in the age group 60–70. Studies by Jonkers[2311], [2312] at the Ophthalmic Clinic of the University of Utrecht during the period 1930–1946, based on 2600 patients, indicated a marked seasonal influence in the occurrence of ruptural retinal detachments in the Netherlands, *i.e.* a rise in the summer months with a maximum in June and a minimum during the winter months. Sixty-one percent of the detachments occurred in patients with myopic eyes. Jonkers' observations were confirmed by the studies of Weekers at Liège, Belgium (in 1945).

A similar study by Jonkers, using 145 reliable anamneses of cases of retinal detachments observed at the Opthalmic Clinic of Bern (Switzerland) in the period 1930–1946, did not disclose any significant seasonal effect. However, studies by Cuendet[2287] in Geneva, based on 218 cases (period 1936–1947), indicated a maximum from March to May and a minimum from

November to January, which proved to be mathematically significant at the 95–99% level.

In view of the many climatological and altitude differences between the Netherlands and Switzerland it is not surprising that the statistical results obtained in the two countries should be different. More research in other countries is required to explain the meteorotropic aetiology of this eye disease.

3. Other, possibly Meteorotropic, Eye Diseases

A number of other eye diseases have been described which seem to be, at least partly, meteorotropic in character. Although most of the conclusions are based on a large number of subjective observations by experienced ophthalmic surgeons, it has not been possible to make a statistical analysis of the weather-disease relationship in most of the reported cases; the conclusions given below, therefore, are submitted with due reserve.

In the period from 1935 to 1938 Dekking[2289] compiled in the Netherlands the daily number of different eye diseases reported in his clinic and compared the days when the complaints started (according to the patient) with the weather conditions prevailing at that time. The following observations were made: *acute conjunctivitis* (*i.e.* inflammation of the membrane lining the eyelids and covering the eyeball) seems to coincide with pleasant sunny weather (74% of all cases). This appears to apply only to the months of May to September each year. *Hordeolum* (*i.e.* infection of a gland of the eyelid) and *blepharitis* (inflammation of the cilia and glands of the eyelid margin) are particularly common during rainy weather (73% of all reported cases). *Keratitis dendritica* (*i.e.* tree-shaped inflammation of the cornea) seems to be very common (in about 82% of all observed cases) a few days after a drastic change in weather (*e.g.* after an approaching depression), comparable with Ungeheuer's weather phase 5 (see p. 24). *Keratitis marginalis* and *scleritis* (*i.e.* inflammation of the sclera) did not show any clear weather relationship. *Phlyctenular conjunctivitis* (*i.e.* severe inflammation of the eye marked by small vesicles surrounded by a reddened zone) usually begins (in 78% of the cases) on cloudy days without sunshine.

In 1934 Hinrichs[2292] studied various kinds of *herpes cornea* (such as keratitis dendritica, keratitis superficialis and keratitis disciformis) at the Ophthalmic Clinic of Greifswald (Germany). It was noted that the observed cases occur in groups. These periods coincided with drastic weather changes (Ungeheuer's weather phases 4 and 5) characterized by frontal passages and steeply falling barometric pressure. Previous studies by Marchesani suggest a seasonal increase of herpes cornea in February and March. According to Hinrichs, *serpiginous corneal ulcer* is most frequent in July and August (based on the period 1923–1932 at Greifswald), but several deviations from this timing have occurred in different years. It is, therefore, doubtful whether this disease is a truly seasonal one. On the other hand, *Diplobacillus conjunctivitis* seems to be a truly seasonal phenomenon at Greifswald, at least it appeared to be so in the period between 1923 and 1932, with a peak in July every year. *Phlyctenular conjunctivitis* was most frequent in Greifswald (period 1923–1932) between Jan. and April (max. in April), which Hinrichs ascribed to the gradual increase in sunlight in early spring.

A similar seasonal relationship was observed by Wessely in 1919, Peyrer in Graz (in 1921), Giallombardo in Palermo (in 1924), Werner in Helsinki (in 1928) and Cheng-Lieh-Wang in Shanghai in 1934. However, the maximum values occurred in Palermo in February, in Graz and Greifswald in April, in Helsinki in May, in Shanghai in July. Wessely, Peyrer and Kassner also believe that lengthening daylight in early spring is responsible for the disease. According to Werner, it is the lack of light in January–April which is the main cause, whereas Giallombardo is inclined to accept the low winter temperature as the main causative agent. The shift in seasonal peak from Palermo to Helsinki seems to suggest a possible sun effect, the more so as the peak appears in these different areas during the time of the year when the maximum height of the sun is about 45°. However, other observations seem to contradict this assumption.

The monthly percentages published by Hinrichs are the following: January 3.9%, February 4.7%, March 5.8%, April 5.9%, May 4.0%, June 1.7%, July 1.3%, August 1.4%, September 2.6%, October 3.0%, November 2.4%, December 1.5%. The difference in sun hours between December and January is very small (roughly 10 hours/month in W. Europe), yet a considerable difference in percentage is observed. It is also surprising that, at least in Graz and Palermo, the percentages of phlyctenular conjunctivitis should increase from November although sunlight is waning in that period. A similar discrepancy is observed in Helsinki. Rohrschneider[2294] is therefore inclined to believe that, as in the case of rickets, it is the *lack of sunlight in winter* which is responsible for the disease. This would also be in agreement with Dekking's observation mentioned above. On the other hand, the maximum in Shanghai is in July, yet Shanghai is on latitude 30° as against Helsinki on 60° (with a maximum in May). The high temperature and humidity in Shanghai and the great height of the sun in July seem to suggest that temperature stress (either extreme cold or heat) may play an important part in this complex disease next to the number of sun hours.

An extensive statistical analysis was carried out by Cuendet and Streiff[2296] for the period 1942–1947, using the records of the Ophthalmic Clinic of Lausanne (Switzerland). The seasonal incidence was studied for various eye diseases (the same as mentioned above). Cuendet considered the periods

January–March, April–June, July–September and October–December. The meteorotropic character of *rheumatie iritis* (*i.e.* rheumatic inflammation of the iris) was stressed for the first time by Enroth in 1932. According to Cuendet[2288], it is most common from April to August (at least in Switzerland), with a maximum around April and a minimum in February and October. Considering the fact that this conclusion is based on only 200 cases in 10 years, no statistical significance could be established.

An interesting study was published recently by Warmbt and Nonnenmacher[2297], based on records at the Ophthalmic clinic of Dresden University (Germany). After operations for cataract, they observed increased *haemorrhages in the anterior chamber of the eye* during certain weather conditions, particularly from January to May. Of the 47 cases in 1957, 30 cases could not be explained clinically. A weather analysis by Warmbt, using Ungeheuer's weather phases (see p. 24), strongly suggests a correlation between haemorrhages and weather phases 2 and 3. The haemorrhages usually take place in the early morning and are more common in females (70%) than in males (30%). According to Le Grand, the haemorrhage is mainly due to a sudden *increase in capillary permeability* and release of a small thrombus which was formed after the cataract operation. Apart from endogenous physiological causes, an increase in capillary permeability is caused by the influx of warm air masses or the passage of warm fronts (see pp. 280 and 335). Elschnig, Carle and Custodis, on the other hand, pointed out that changes in permeability are probably not the main cause of haemorrhages. They believe that increasing interocular pressure after an eye operation causes a rupture of the newly formed tissue fibres. This mechanism would be corroborated by the observation that many haemorrhages at Dresden apparently occur during the passage of very active cold fronts with great air turbulence and the influx of polar air. However, as clearly stated by Warmbt, the observed relationships are not highly significant from a statistical point of view.

This brief summary of the various biometeorological studies, in relation to eye diseases, which have been published during the past 50 years, has shown that a considerable amount of research has been devoted to this problem, but much remains to be done to account for all the observed statistical relationships.

Subsect. D. LUNG DISEASES

In this section only two, apparently meteorotropic, lung diseases will be briefly discussed, *viz.* bronchitis and tuberculosis of the lung.

1. *Bronchitis*

Bronchitis is a disease set up by inflammation of the bronchi as a result of air pollutants or infectious agents (*e.g.* influenza virus, pneumococci, etc.) It is more common in males than in females and seems to run in certain families. The clinical manifestations are largely due to bronchial obstruction caused by tenacious sputum which cannot be removed sufficiently by the cilia of the trachea.

The inability of infants and aged persons to empty their bronchial secretion accounts for the high incidence of broncho-pneumonia at the two extremes of life. The death rate varies considerably in different countries. For the same age group it is, for example, ten times higher in England than in Denmark.

Acute bronchitis is usually characterized by fever, sweating, coughing, substernal pain, choked-up feeling, paroxysms of dyspnoea following spells of coughing. *Chronic bronchitis* is a chronic affection of the bronchi and bronchioles causing a prolonged cough, which is usually exacerbated by a change in the weather. A special form of bronchitis is known as *asthmatic bronchitis*. It is the result of the rapid accumulation of secretion during an acute asthmatic seizure and the associated swelling of the mucosa, causing severe dyspnoea, a wheezy chest and an unproductive cough. Fever is due to secondary infection.

Various studies on the influence of weather and climate on bronchitis have already been discussed in the preceding chapters.

The geographical distribution of bronchitis-pneumonia in the Netherlands was reviewed on p. 159 when dealing with the medical-geographical method. It was pointed out that, contrary to the general assumption, the highest mortality occurs in the Eastern part of the Netherlands, the Western part near the North sea being lowest. The difference in climate between the two areas was summarized on p. 26. The Western part is located on moist clay soils; topographically, the Eastern part is usually rather higher and consists mainly of sandy soils. Less air turbulence in the Eastern part of the Netherlands (due to meteorological factors and ampler forestation) and the greater porosity of the surface layers of sandy soils there, are responsible for the prevalence of foggy days spread over the year in that part of the Netherlands. The N.E. - S.W. separation line as described on p. 159 suggests that differences in weather conditions between the areas East or West of this line are mainly responsible for the geographical distribution of bronchitis mortality in the Netherlands.

The 1954 studies by Pemberton and Goldberg[201], indicating a steady increase of bronchitis from rural areas to the cities, were discussed on p. 99. Death rates from bronchitis of males of the age group 45–64 per 100,000 of the male population of England and Wales in 1953 were 61 in rural districts against 114 in cities of 100,000 inhabitants and over; for females the same figures were 17 and 32. It was pointed out that experiments by Amdur *et al.*[2328] in 1953 and by Cralley suggest that the increased SO_2 content of the air of most industrial cities may be, at least partly, responsible for a decrease in ciliary activity of the human trachea. Pemberton drew attention to a statistically significant relationship between average SO_2 content of the air in the different counties of England and mortality rates for bronchitis in men aged 45 and over. However, it should be borne in mind that certain meteorological factors which may actually be responsible for an increase in bronchitis may also increase the local SO_2 content of the air. Therefore the observed SO_2 correlation may not necessarily be causal. The fact that bronchitis mortality in the Western, most industrialized parts of the Netherlands is low would appear to support this view. On the other hand, recent studies by Goodman, *et al.*[2329b] have shown that the areas of high bronchitis mortality in England lie to the North of a line drawn from Bristol to the Wash, representing areas of high industrial activity with considerable air pollution. Apart from SO_2 and other pollutants, ionisation may be involved. It was pointed out on p. 361 that, according to Krueger *et al.*, a surplus of positive ions, especially in an atmosphere rich in CO_2, may lower the ciliary rate considerably, causing nasal obstruction, dry, scratchy throat and so on. As these conditions may prevail in industrial cities, this is another factor that should be taken into account.

In Boyd's studies[3190] (reviewed on p. 250), a close association was found in the London area, from 1947 to 1954, between the weekly deaths from respiratory diseases of people of 45 and older and temperature and humidity in the preceding week; mortality increased with falling temperature, particularly below 32° F during thick fog. Such periods are usually characterized by an increase in SO_2 of the air. SO_2 in very humid air will change into droplets of H_2SO_4, which may be responsible for the inflammation of the bronchi. Recent studies by Martin and Bradley, at the Ministry of Health, confirmed this observation. During the period from November 1958 to February 1959 a marked increase in bronchitis mortality was observed on days of thick fog (*i.e.* visibility less than 450 yards). A significant positive association was found between the black suspended matter in the atmosphere and the daily number of deaths.

Lawther[2335, 2336] and his colleagues studied for many years the influence of environmental factors on bronchitis at St Bartholomew's Hospital in

London. One of the interesting observations in January 1955 was a period of heavy "smog" which seemed to be free from sulphuric acid, at least as estimated by the methods used; nevertheless, a temporary marked deterioration of many chronic bronchitis patients was observed. The studies were repeated in January 1956 with 180 patients living in Greater London. It was found that practically all days with sharp peaks in smoke (and SO_2) concentration coincided with marked peaks in the degree of illness of the patients. Many patients are affected before wet fog is formed. Fog may even be absent during such a period of deterioration of health if there is still a high concentration of smoke. Lawther suggested that, in the event of low relative humidity, the droplets may possibly be smaller (*e.g.* 1 μ), when the H_2SO_4 concentration and its effect is greater than during dense wet fog with droplets of 20 μ and low H_2SO_4 concentration. The various factors affecting the penetration of aerosols, as described on p. 301, should also be considered in this connection. Lawther pointed out that the *close relationship between smoke concentration and degree of illness of bronchitis patients* is only true for the winter months. It seems to disappear in spring and summer. This suggests that other factors must be involved apart from air pollution, a conclusion supported by the geographical distribution of this disease in the Netherlands, described above. Also the fact that considerably higher morbidity and mortality are found for males than for females (the ratio often being 3 to 1 or more), even among office workers living in the same area, strongly suggests that air pollution alone cannot account for the observed phenomena. The familial aspect of the disease likewise supports this view. There may be a fundamental difference in susceptibility between the lungs of males and females, as suggested by the studies made by Brimblecomb *et al.*[2329a]. It seems that, at least in London, the female is more susceptible in early adult life to respiratory infection than the male. The opposite may apply in later life. On the other hand, Oswald and Medwei noted differences in smoking habits between males and females in the same occupational group of Civil Service Clerks.

Considerable research work on the effect of environmental factors on bronchitis was carried out by Reid and Fairbairn[2338a, b] at the London School of Hygiene and Tropical Medicine. Reid studied the medical records of 565 postmen retired prematurely because of chronic bronchitis during the period 1950–1954. They were matched with similar age groups of postmen still in the Service. The following results were obtained: (*i*) Postmen who were ultimately disabled or who died prematurely from chronic bronchitis had more and longer absences than their controls even in early adult life. (*ii*) After the age of 45 the "bronchitics" had 8–10 times more attacks of pneumonia, pleurisy and asthma than their "controls". (*iii*) Bronchitics have more disability from peptic ulcer and more deaths from coronary disease and lung cancer, which may be due to the fact that, apart from smoking, various stress conditions and overstimulation of the autonomic nervous system play an important part in the development of bronchitis. (*iv*) Bronchitics above the age of 45 suffered most from bronchitis, pleurisy and pneumonia in the areas of the United Kingdom with the highest fog frequency and degree of air pollution. This correlation was more consistent than with temperature. Also the bronchitis ratio between postmen and clerks (working indoors) became larger in the areas with high fog frequency and high degree of air pollution. (*v*) In the London area the invaliding-rates from chronic bronchitis for London postmen (working under the same material conditions and practically the same environmental temperature and humidity) rise steadily from South-West to North-East. A similar relationship was found for lung cancer mortality. It also coincides according to Wilkins with the build-up of smoke in the Greater London Area by the prevailing West-South-West wind.

Reid summarizes his observations as follows: "In a stable group of men, doing the same job for the same pay under the same conditions of service, there are wide geographic variations in the incidence of disabling respiratory disease, variations which cannot be explained by social, economic or occupational factors or by any other consistent difference in climate other than fog".

The foregoing summary of the most important bronchitis-weather studies indicates that the actual primary cause of bronchitic attacks is still unknown. For all that, a number of interesting weather relationships have been found: (*i*) Whereas the frequency of asthma attacks in asthmatics, suffering from pure bronchial asthma, decreases during foggy periods (see p. 467), the condition of the bronchitic person becomes worse. This shows that certain asthmatics appearing to be affected by fog are in effect suffering not from bronchial asthma, but from asthmatic bronchitis (see p. 464). The effect of hypotonic aerosols in fog will be discussed on pp. 634 and 651. (*ii*) In industrialized areas with high CO_2 and SO_2 contents of the atmosphere, foggy conditions apparently reduce the ciliary activity of the trachea, either through the formation of H_2SO_4 droplets or on account of a surplus of positive air ions. Depending on the size and electric charges of the fog droplets, the environmental agents can penetrate to different depths. (*iii*) The susceptibility of the lungs of bronchitics to these external agents seems to decrease in spring and summer, probably because of the rise in environmental temperature (which reduces foggy conditions) and because of increased resistance of the body to infectious diseases (see p. 511). (*iv*) In non-industrialized areas, the cooling effect of fog may increase the capillary resistance of the membranes of the respiratory system and reduce the blood flow to these parts of the body, thus favouring the growth of infectious agents. (*v*) It may be that people with a hereditary or subsequently acquired unbalanced autonomic nervous system are more susceptible to these various weather effects, considering the greater proneness of bronchitics to peptic ulcer and coronary disease. In the opinion of the author, it is doubtful whether differences in smoking habits alone could account for this tendency, as suggested by many research workers.

2. *Tuberculosis*

Although the favourable effect of heliotherapy and mountain climate on certain forms of tuberculosis was early recognized, particularly by the Swiss physician A. Rollier (1915), the development of antibiotics in recent years and their application to the treatment of tuberculosis have tended to divert the attention of many physicians from the meteorotropic aspects of this disease. Space prevents me from reviewing the complete literature on this subject (see, for example, refs.[2313 2393]). Only a few important points will be briefly discussed.

Mechanism of the development of tuberculosis

Although the tubercle bacillus, the actual primary cause of infection, can implant itself in any part of the body, usually (in more than 90% of the cases) the seat of the primary infection is in the lung. High-speed photography has shown up innumerable droplets of fluid expelled from the nose and mouth of an infected person sneezing or coughing. The smallest of these droplets quickly evaporate, leaving minute particles of germ-laden matter floating in the air, which can be aspirated by others into the lungs (see p. 520). Following the inhalation of such sputum, droplest or dust particles, which need contain only a few living tubercle bacilli, a patch of bronchopneumonia develops near a small bronchus. After a few days, while the bacilli grow, an inflammatory reaction is created to which the lungs respond by pouring out polymorphonuclear leucocytes, red blood cells, etc. Monocytes and lymphocytes appear subsequently and the infection spreads by way of the lymphatics to the lymph nodes in the lung. Only under certain constitutional and environmental conditions may this give rise to destructive changes. For example, according to E.H. Rubin, in the U.S.A. about 70 million people have been infected, but only 600,000 are struck down with clinicial tuberculosis. Furthermore, differences in geographical distribution of this disease suggest the importance of environmental factors, such as social conditions (affecting general resistance and contact facilities), racial differences, climate, etc. Races that have been in contact with the tubercle bacillus for many centuries (*e.g.* Italians or Jews) seem to have acquired greater resistance and the disease has a better prognosis. On the other hand, Negroes, American Indians and Eskimos appear to develop more acute and progressive tuberculosis.

About six weeks after infection, an allergy develops (see p. 460), which is determined by the *tuberculin test, i.e.* a heightened sensitivity of the tissues to products of the tubercle bacillus (particularly the protein fraction) after injection of extracts of tubercle bacilli. In severe stages of tuberculosis, *haemoptysis* may occur, *i.e.* spitting blood as a result of sudden dilatation of the pulmonary and bronchial arteries during acute lung infections (*e.g.* pneumonia).

Examples of meteorotropic effects

(1) *Scar pains.* Several physicians in sanatoria have reported scar pains in the lungs of tuberculous patients during changing weather conditions.

(2) *Haemoptysis.* Some authors have reported on the simultaneous occurrence of haemoptysis in a number of patients in the same sanatorium, without any obvious clinical cause (see refs.[2355, 2387, 2388]). Gabrilowitsch, Pottenger, Lansel and Unverricht observed a correlation between a steep fall or rise in barometric pressure and an increase in cases of haemoptysis. According to Schröder[2387, 2388], they are particularly common when these barometric changes are accompanied by changes in temperature and humidity. Therefore, oppressive warm weather before thunderstorms, foehn weather (see p. 24), very humid cold foggy weather in winter or sudden heat waves in summer may trigger off attacks of haemoptysis. Although the detailed mechanism is not yet known, it is very likely that disturbances of the thermoregulation mechanism are mainly responsible for these phenomena.

(3) *Sensitivity to tuberculin test.* Ossoinig[2384] reported in 1926 on seasonal variations in sensitivity to the tuberculin test, *i.e.* an increased sensitivity in March and April and a low sensitivity during autumn. Similar observations were made by Karczag, Arnfinsen, Hamburger and Peyrer (see p. 587). During daily tests on children, too, a sudden increase in sensitivity was sometimes observed, either in all the children or at least in the majority of them. Studies by Heuss suggest that such days are related to the passage of weather fronts.

(4) *Seasonal fluctuations of tuberculosis.* De Rudder[2355] reported on a number of seasonal fluctuations of different forms of tuberculosis. (*i*) In northern countries tuberculosis mortality increases in spring with a maximum in May. Also the severity of tuberculosis morbidity is highest in May, particularly in the case of lung tuberculosis. This fact is consistent with the observation made by Orszag and Strandgaard[2391], to the effect that the results of sanatorium treatment are least satisfactory in spring, whereas the best results are usually obtained in summer and autumn. For the same reason, according to Ernst[2359–2361], operations on tuberculous patients in spring are best eschewed. (*ii*) Hartwich observed the same in miliary (pulmonary) tuberculosis. Redlich, Koch, Holt, Albinger and Wangenheim noted a similar peak for tubercular meningitis (*i.e.* acute hydrocephalus), the mortality from which in spring is 3.5 times that in late summer. (*iii*) From 1920 to 1929 von Malinckrodt–Haupt[2381a] observed fluctuations in the complaints of patients suffering from *lupus vulgaris* (*i.e.* tuberculosis of the skin) in the University Clinics of Bonn, Cologne and Düsseldorf (Germany), with a maximum in February and a minimum in September. This conclusion was based on 1531 cases.

(5) *Thalassotherapy.* The influence of this therapy has been reported by Haeberlin[2369–2375] and others. The biological effects of sea climate will be discussed more fully on p. 644. (*i*) Haeberlin[3891a, p. 158], Czerny and others have stressed the fact that lung tuberculosis and serious cases of chronic bronchitis should *not be treated in sanatoria on the sea coast,* mainly because of the generally prevailing air turbulence and cooling effects near the coast. The unfavourable effect of excessive ultraviolet radiation was discussed on p. 339. (*ii*) According to Haeberlin[3891a], p. 135) and Kalkoff[2376], the combined effect of great air turbulence, high humidity and high radiation intensity* on the sea coast is favourable for the treatment of *skin tuberculosis* (*e.g.* lupus vulgaris). Owing to the strong cooling effect of the sea breeze, the heating by infra-red radiation is reduced and therefore excessive vasodilation and peripheral overstimulation are prevented. (*iii*) Haeberlin reported on 128 children suffering from *abdominal tuberculosis* who received climatic treatment in 1948 at the sanatorium of Norderney (Germany). They were completely cured in a year to 18 months. (*iv*) *Osteotuberculosis* (comprising caries fungosa or tuberculosis of the bone and tumor albus or tuberculosis of the joint) has been successfully treated in various European countries at seaside sanatoria. In the United Kingdom, such climatic treatments were

* Due to reflexion of sand and water, the reflected solar energy, particularly of the shorter ultraviolet rays, may be twice that from a field of grass in the case of water; four times in the case of sand; 8 times in the case of snow.

applied at Margate as far back as 1796. In France they have been tried since 1896 at Berck; in Germany since 1906 at Sahlenburg/Cuxhaven, Norderney and Wijk. In France, more especially, thalassotherapy has been successfully applied by Ménard and Calvé on the N.W. Coast, bordering the North Sea (not on the South or West Coast). The saying "La cure marine règne en maîtresse sur les tuberculoses osseuses" is familiar to French surgeons.

According to Treplin, in 1925 chief surgeon at Sahlenburg, not only surgical cases of osteotuberculosis, but various chronic infections, rickets and osteomyelitis, requiring surgical treatment, are successfully cured on the North Sea Coast. Here, the best results have been reported *during the winter season* when there is little sun and much wind, suggesting that sun radiation is not a direct factor in this particular treatment. This bears out our previous statement, concerning seasonal phenomena, that mortality from tuberculosis and the severity of patients' complaints reach their peak in spring. Brannan (in the U.S.A.) and Bradford also reported that the best results were obtained during cold weather in winter. Studies by Hill in 1925 suggest that in the course of climatic treatment in winter the metabolism of the patients increased by 30% as compared with experiments in summer. Further study is required to discover what physiological mechanisms are involved. In the present state of our knowledge it is difficult to tell whether success is mainly due to the lowering of temperature, with the accompanying changes in endocrinal functions of the pituitary, (see p. 259), or to the regular seasonal changes of many physiological functions in our body, such as growth, etc. (see p. 575).

(6) *Conditions for lung sanatoria.* Whereas in the beginning of the 20th Century most physicians favoured a cure in mountain climate, the results obtained at sealevel in W. Europe indicate that climates favourable for lung tuberculosis can also be found at low altitudes. The main conditions required for lung sanatoria seem to be the following: location on dry, well drained, soil high above the ground water level, in the middle of forests (preferably pine forests), far from the sea coast, in an area with few foggy days. Forests prevent direct sunlight to reach outdoor patients and reduce reflected solar radiation; absecence of dust or other chemical air pollutants and little air turbulence are other favourable aspects. Whether the difference in electric properties of the atmosphere (*e.g.* low potential gradients in forests) may play a part is not known yet.

Subsect. E. HEART DISEASES

In references[2394-2425] a summary is given of the most important studies on the influence of weather and climate on various heart diseases, in particular *coronary thrombosis* (formation of a blood clot within the heart or in one of the coronary arteries of the heart), *myocardial infarction* (development of an acute local deficiency of blood supply in the cardiac muscles, usually due to a blood clot, followed by injury of the cells and usually involving the left ventricle of the heart), *angina pectoris* (paroxysmal thoracic pain, usually radiating to neck and left arm and due to spasms of the heart muscles and temporary insufficient blood supply), and death through *heart failure*. As a considerable percentage of the total mortality figure represents death from heart diseases, the reader is also referred to the section on weather and general mortality on pp. 250 and 571.

1. Observed Meteorotropic Relationships

Studies by Bartels[2397], Beljajen[2400], Kisch[2411], Kolisko[2412] and others strongly suggest a meteorotropic relationship between passages of weather fronts and the increased occurrence of these diseases. The studies of Amelung *et al.*[2395], Fladung[2406] and Ströder *et al.*[2420] in Germany, in particular, have given considerable statistical support to this observation. From 1948 to 1950 Fladung and Becker studied 100 cases of sudden heart failure, observed in the medical clinics of the University of Frankfurt (Germany), of which the cause and the hour of death were exactly known. Most cases were due to coronary thrombosis and myocardial infarction. A mathematical analysis showed a statistically highly significant correlation with the passage of weather fronts (99.99%). In 1951, Ströder *et al.*[2420] showed that 87% of 63 cases of myocardial infarction followed by sudden heart failure, of which the exact diagnosis was established electrocardiographically and afterwards by autopsy, occurred on days of *considerable meteorological disturbance* characterized by the *passage of active weather fronts*, either cold or warm.

Studies by a number of authors indicate a clearly *seasonal incidence* of both morbidity and mortality from arteriosclerotic heart diseases. Wood and Hedley[2425] studied 133 electrocardiographically established cases of coronary thrombosis (not immediately followed by death), covering the period 1932–1934, at the University of Pennsylvania (U.S.A.). For each of the three years the highest values were found in autumn and winter, the lowest in spring (March–May) and summer, with a clear minimum during June, *i.e.* before the summer holidays may affect the number of potential patients in Philadelphia. According to the Bureau of the Census in Washington DC., 27,390 cases of angina pectoris and coronary heart diseases occurring in 1933 showed a similar seasonal relationship. The same seasonal incidence was established by Master[2415a] in New York, by Bean[2398a] in Boston, by Mullins[2415c] in Pittsburgh, by Bean *et al.*[2399] in Cincinnati, by Mintz and Katz[2415b] in Chicago, by Miller *et al.*[2415] in Rochester, by Hoxie[2409a] in Los Angeles and by Billings *et al.*[2400a] in Nashville.

A similar study by Koller[2413] in 1937, at the Statistical Department of the W.G. Kerckhoff-Herzforschungs-Institut of Bad Nauheim (Germany), using 1,600,000 mortality data of the United Kingdom (period 1921–1933), showed a clear maximum of arteriosclerotic heart diseases in January-February with a minimum around July–August. No difference between males and females was observed despite the great difference in total mortality from heart diseases.

All these studies were carried out in Northern climates with temperate summers. However, studies by Heyer *et al.*[2408] in Texas, where the summers were very hot, showed a different picture. It was found that acute myocardial infarction in Texas is more frequent during the hottest season of the year, *i.e.* during July and August, with maximum temperatures often exceeding 100° F, and with moderate humidity (60–70%). During the rather mild winters in Dallas, with an average minimum temperature during January of 35° F, the incidence of myocardial infarction is low. The conclusion was based on 1386 cases observed during the period 1946–1951 in Dallas, Texas, of which the clinical record, electrocardiograms and exact time of onset were known.

Further meteorological studies by Teng and Heyer[2421], using the same material, showed a statistically significant increase in incidence of acute myocardial infarction during or immediately after the sudden inflow of polar or tropical air masses, causing fluctuations in temperature of 36° F, up to 62° F in cases of cold air masses. In other words, the increase occurred during periods of drastic meteorological changes. The increase was considerably greater in the case of cold air influxes, which are particularly common in Dallas between October and April. The vast majority of these patients suffered the onset of their illness while asleep or at rest, from which it may be inferred that physical activity was unlikely to have been an important factor in these cases.

Heyer's facts appear to contradict the overwhelming evidence in Northern regions of the highest incidence in winter. Tromp[2422], however, has been able to show that both phenomena may occur in the same area even at Northern latitudes. A statistical study in the Netherlands of mortality from angina pectoris, coronary thrombosis, myocardial infarction and apoplexy for each year in the period of 1935 to 1958 points to the following: (*i*) Mortality is highest in January–February (usually the coldest months of the year in the Netherlands) and lowest in July–August. Winters with abnormally low temperatures are characterized by very high mortality, warm winters by relatively low mortality but still considerably higher than in summer. (*ii*) There is an almost perfect inverse relationship for all the months of the year between the curves representing the average monthly temperature and the mortality from arteriosclerotic heart diseases. Some physicians have tried to account for the high peak in January and February by the increased exertion of snow shovelling imposed on heart patients. This may be true in certain parts of N. Europe, Canada and the Northern U.S.A. but definitely does not apply to most West-European countries. The population of these parts of the world is usually more active in spring and summer when many older people are engaged in light sports or gardening. (*iii*) The generally low mortality figures in summer are highest during the warmest summers, which are often accompanied by short spells of heat waves. (*iv*) During years with a double temperature minimum, *e.g.* the winter of 1943–1944 with a temperature minimum both in December 1943 and February 1944, a double peak in the heart mortality curve is observed, both in December and February. (*v*) There is usually little difference between the monthly mortality curves of the male and female population; only the total percentage of females who die from apoplexy is higher than that of males, whereas the reverse is true for angina pectoris, coronary thrombosis and related heart diseases.

These observations suggest that both hot and cold stress increase the mortality from coronary thrombosis and related heart diseases.

2. *Possible Meteorotropic Mechanisms Involved*

The vast material collected leaves no room for doubt that there is a significant causal relationship between climate, weather and mortality from the heart diseases described above. The actual physiological mechanisms involved, however, are not yet known with certainty. The heart diseases described are particularly common among people suffering from severe arteriosclerosis or a very unbalanced autonomic nervous system (either heriditary or as a result of constant stress conditions in life, involving the emotions, or caused by heavy responsibilities in the world of business, etc.). We have seen that both extreme cold and heat may bring about considerable dysfunction of the thermo-regulation mechanism of the human body and of all the endocrinal and nervous functions in the body controlled by the hypothalamus. As a result, profound circulatory alterations occur (see, *e.g.*, p. 217), which may cause an over- or under-stimulation of the heart-muscles. This may be detrimental if the functioning of the heart is a labile mechanism, as in the case of potential heart patients, *e.g.*, persons suffering from severe arteriosclerosis. A dysfunction of the thermo-regulation mechanism probably implicates three important processes as contributory precipitants of these heart attacks, *viz.*,

(1) *Dysfunction of the autonomic nervous system* causing vasomotor reflexes. It was pointed out on p. 574 that in a healthy population group the average blood pressure increases in the winter months, the capillary resistance being high and affecting the blood pressure and peripheral resistance of the arteries.

(2) *Changes in the physico-chemical state of the blood,* such as viscosity, sedimentation rate, coagulation time. (*i*) During the cold winter months, at least in the Netherlands, the blood sedimentation rates of healthy people are lower than in summer (see p. 318), probably due to changes in fibrinogen content, although this has yet to be confirmed. On p. 319 it was pointed out that studies by Caroli, Halse and Losnitzer indicate that considerable changes in the fibrinogen content of the blood are related with cold fronts. (*ii*) Stress conditions and increased adrenalin secretion increase blood viscosity and shorten coagulation time (see p. 316). The experiments of Caroli and Pichotka were described on p. 319, indicating a shortening of the coagulation time before the passage of warm and cold fronts, but in particular shortly before the passage of a cold front.

(3) *High capillary fragility.* On p. 577 it is pointed out that during winter the capillary fragility is usually high (at least partly due to vitamin P deficiency), which seems to cause the higher incidence of cerebral haemorrhage in newborn infants during winter. Similar mechanisms may be involved in the high incidence of meteorotropic heart diseases and apoplexy during winter.

Although it is difficult at the present stage of research to determine exactly how these different factors bring about a myocardial infarction, coronary thrombosis, etc., one or more of the mechanisms described are most probably involved during the specific weather stress causing high mortality from these heart diseases. In this connection it is worth mentioning that recent studies by Héroux and Campbell in Canada (Lecture 5th Gerontological Congress, San Francisco, August 1960) show that rats exposed to 30° C have a longer life-span and suffer less from cardiovascular diseases than rats exposed to temperatures down to 6° C.

The effect of weather and climate on arteriosclerotic heart diseases is also modified by ethnological differences, as pointed out by Dreyfus [2403] and others. It is a well-known fact that considerable differences exist in the type and degree of arteriosclerosis afflicting different races. In 412 cases

Dreyfuss noted the highest incidence of myocardial infarction among Jews stemming from the East and Central and Western Europe, the lowest figures being found among the Oriental Jews originally settled around the Eastern Mediterranean. Both groups lived for many years in Israel under the same climatic conditions, but their genetic, social, nutritional and psychological stress patterns are different (*e.g.*, hypertension is rare in the Oriental Jew). Considerable variations in the incidence of arteriosclerotic heart diseases can therefore be expected, even in the same country with the same climatic and weather conditions, if considerable ethnological differences prevail.

The main result of the studies described could be used succesfully for preventive purposes and for future meteoro-pathological forecasting. Patients suffering from arteriosclerotic and related heart diseases should try to live, at least during very cold or very hot seasons, in areas with a mild climate and not normally subject to great atmospheric turbulence. If this is not possible for financial or other reasons, they should protect themselves in winter by staying at home on very windy days and, in particular, just before and after passages of weather fronts. Although meteoro-pathological forecasting in this connection might have undesirable psychological effects, gradual education of the general public by radio and television may overcome this difficulty and might well extend the life-span of many heart patients. Needless to say, that serious operations, especially heart operations, should, for the same reason, be postponed for a few days, if possible, till less turbulent air conditions have set in.

Subsect. F. INFECTIOUS DISEASES

The possible influence of weather and climate on infectious diseases is a very complex problem, but, although it is one that has been studied widely and most scientists accept such a relationship, very little is yet known about the exact mechanisms involved. Space prevents me from discussing all the aspects which have been studied during the last 50 years. The interested reader is advised to consult the refs.[2426-2547]. The factors involved in the contraction of infectious diseases, as a result of specific weather and climatic conditions, can be classified into two large groups: Factors causing a lowering of the resistance of the human body to infection and those affecting the ease of spread of an infection. This latter group can be divided into at least three important sections, *viz.,* influence of weather and climate on the social habits of man (such as crowding in rooms, shutting of windows and doors, changes in clothing, food etc. during certain seasons), influence on the development of micro-organisms and viruses and on the spreading of these infectious agents through the air.

Space does not permit discussing the influence of weather and climate on the social habits of man. The other factors will receive brief attention in the ensuing pages, followed by a very short review of a few important infectious diseases: angina, common cold, diphtheria, influenza, poliomyelitis, scarlet fever and whooping cough.

1. Influence of Weather and Climate on the Resistance of the Body

Whereas most epidemiological studies seem to concentrate on the causes and prevention of the spread of infectious diseases, relatively few studies have been devoted to the problem of the effect of weather and climate on the resistance of the body. Everybody knows from personal experience that sometimes one may be exposed to infection from a number of people suffering from various stages of the common cold or influenza with complete impunity, whereas at other times the presence of only one such person, even for a short period, is enough to infect one with the complaint. The same applies to other infectious diseases. This phenomenon is accounted for by *body resistance*.

We distinguish between two kinds of resistance, *viz., local resistance* (affecting the place of entrance of micro-organisms or viruses in the body and the place of settlement and further development) and the *general resistance*. Physico-chemical and structural changes are apparently involved in both types of resistance.

Biometeorological factors affecting local resistance

(1) *Influence on permeability of membranes.* It was pointed out on p. 335 that climate and weather affects the capillary resistance and permeability of the membranes and the peripheral blood flow. This may facilitate the penetration of micro-organisms through the various membranes of the body cavities.

(2) *Influence on acid coating of the skin.* The experiments of Heinke and Hermann discussed on p. 100 suggest that alkaline aerosols in the atmosphere may affect the acid coating of the skin which acts as a protective layer against micro-organisms. The existence of such an acid coating on the skin was demonstrated by Marchionini[2445a] as far back as 1928. In a series of experiments in 1938 Marchionini *et al.*[2446-2448] proved the significance of this acid coating as a defensive layer against bacteria.

The acid coating is produced by the secretion of the *eccrine sweat glands* (see p. 216) followed by evaporation. During secretion, the pH of the fluid fluctuates between 4 and 6; after evaporation between 3 and 5. Marchionini noticed that certain spots on the human skin have a very low acidity or may be even alkaline. They represent *physiological gaps* in the acid coating and may be favourable areas for the growth and penetration of micro-organisms through the skin. These alkaline spots are due to secretion of the *apocrine sweat glands*. The sweat of these glands is only slightly acid or even neutral and becomes alkaline after evaporation, contrary to eccrine secretions. Owing to the alkaline fluids, the keratin colloids of the outer horny layer of the epidermis become swollen (see p. 209), thereby reducing the firmness and resistance of this upper skin layer. Lack of evaporation of sweat (even eccrine) between skinfolds (especially in obese persons) will also change the coating within 24 hours into an alkaline layer, mainly owing to the formation of NH_3 by bacterial action. Marchionini demonstrated the destructive effect of the acid coating experimentally (and showed that these alkaline spots favour the growth of bacteria and fungi) by placing pathogenic micro-organisms on these spots on the skin of 31 healthy adults and of 9 healthy children. These experiments also demonstrated that, except on the abdomen and the back, the very acid areas of the skin are characterized by few varieties of bacteria, whereas on the slightly acid, neutral or alkaline spots a great variety in micro-organisms is found. Marchionini's observations, which have been confirmed by a number of other research workers, indicate that *all weather conditions affecting the sweating rate and evaporation* (such as temperature, humidity, air movement) *may influence the growth of micro-organisms* on, and their penetration into, the skin. Apart from these meterological factors, the intensity and dominating wavelenghts of the ultra-violet sun radiation also play an important part in the destruction of micro-organisms on the human skin (see p. 518), particularly at high altitudes. It is consistent with what has been said that *hot thermal baths*, followed by cooling and undisturbed evaporation of the sweat, tend to increase the acidity of the skin and, therefore, to cure some bacteriological and mycological skin diseases.

(c) *Influence on dryness of membranes (esp. nasal mucosa)*. Several authors have pointed out that certain conditions of temperature, humidity and ionization of the air may affect the dryness of the membranes, particularly of the nasal mucosa. Dryness and cooling may cause micro-fissures in the epithelium. (*i*) Attention was drawn on p. 356 to experiments by Krueger and Smith which showed that a surplus of positive ions may produce dryness of nose and throat and reduce the ciliary rate of the trachea (*ii*) Lawrence [2444a], Proetz[2449a], Hope Simpson[2439c], Waddy[2457a, b, c] and others have stressed the influence of low air humidity (see p. 519). Inspired air is humidified in the body to 95% as a result of the high internal temperature. The required water vapour is withdrawn from the body cells. The drier the inspired air, the greater the desiccation of the nasal mucosa. This occurs especially on col cold frosty days and in central-heated rooms. (*iii*) Excessively prolonged cold induces constriction of the peripheral blood capillaries. The decreased blood flow may cause a similar drying and cracking of the nasal mucosa, as pointed out by Hill *et al.* (*iv*) Armstrong[2520-2523] (see p. 531) and Martini[2448a] stressed the significance of humidity on the secretion of the nasal mucosa. Armstrong was able to show that greater secretion of the mucosa runs parallel with increased concentration of antibodies in the nose (see below). In cold weather the inspired air will drop in relative humidity because of a steep rise in temperature. This stimulates secretion of the nasal mucosa. The gradual drying and evaporation of the membranes in cold air of low humidity tends to concentrate these antibody secretions. According to Howitt and Bell[2439d, e] the content of antibodies in nasal secretions goes parallel with the serum level. They could demonstrate the presence of specific antibodies against poliomyelitis virus in nasal secretions of poliopatients. (*v*) Experiments by Dowling *et al.*[2439a] on healthy people, artifically infected with the nasal secretion of patients suffering from the common cold and confined in rooms at constant temperature and humidity, showed no differences in proneness to catch a cold between groups kept at different but constant temperatures and humidities. Studies by Hill[2439b] and Article[2427a] suggest that, during war, soldiers do not often contract a common cold, despite the fact that they are subject to great changes in temperature and are crowded together. These observations have been used as an argument against the influence of temperature on local resistance. Those who advance that argument, however, overlook the fact that a person constantly living under great changes in temperature is usually blessed with a better thermoregulation mechanism than others. Also, as will be explained below, the greater stress under which soldiers live may affect their general resistance. Moreover, when, as in the experiments described above, the temperature to which a person is exposed remains constant, acclimatization brings a different mechanism into operation. Neither observation therefore, would appear to affect the previous conclusions concerning the effect of temperature and humidity.

(4) *Influence of ozone.* Experiments of Miller and Ehrlich[141], described on p. 92, indicated a lowered resistance of mice to respiratory infections if they were exposed previously to high concentrations of ozone in the air.

Biometeorological factors affecting the general resistance

(1) *Indirect effect of weather and climate.* This effect is known from animals

more specifically because these meteorological conditions affect the types of nutrition consumed at different periods of the year and therefore influence various metabolic disorders and the incidence of disease resulting from trace element deficiencies. Furthermore, since the abundance and stage of growth of poisonous plants and fungi depend upon the weather, their consumption by cattle in summer may lead to disease and lowered resistance in livestock. This seasonal effect may also be an important factor in man, because in W. Europe more unboiled vegetables are consumed in summer; on the other hand, the greater consumption of various kinds of cabbage in winter often brings on gastric disorders.

(2) *Direct effect of weather and climate.* This effect has not been studied extensively by epidemiologists despite the fact that several studies in related fields suggest an association of the kind.

Pharmocological experiments (see p. 591) have shown that the effect of the same chemical substance can be entirely different if administered under different meteorological conditions; in other words, the body's resistance to these substances varies considerably. In this connection the experiments of Thompson (1938), Parker (1942), Mykytowicz (1956) and Marshall[2448a] in Australia are most elucidating. They showed that rabbits held at summer temperature (26-39° C) escaped infection after inoculation with a dose of myxoma virus, which was fatal if applied during winter temperatures (—3 to 15° C).

Studies by McDonagh in London suggest that the *physicochemical state of the blood,* even of healthy people, changes continuously, not only daily, but monthly and from one year to another. Detailed studies by Tromp at Leiden (the Netherlands)[549] since 1955 have confirmed this assumption. On pp. 286 and 318 it was briefly pointed out that in a healthy group of blood donors the albumin and globulin contents of the blood serum change. Both are short-term changes related to the influx of cold or warm air masses and seasonal changes. The same holds for the various physico-chemical factors affecting the blood sedimentation rate and blood coagulation. It is a well-known fact that *gamma globulin* is an important factor in the phenomenon of immunity to infectious diseases. Therefore, changes in globulin level may affect the general resistance of the body. Important studies on the influence of weather on the physico-chemical state of the blood were carried out recently by the German physician Assmann, in co-operation with the meteorologist Warmbt, at the Medical Clinic of Dresden University (to be published in the Congress Proceedings of the International Biometeorological Congress, London, 4–10 Sept. 1960). The daily fluctuations in blood coagulation properties were studied for 28 days in eight healthy people by means of recalcification, heparin tolerance, prothrombin tests, etc. Statistically significant fluctuations were found in the coagulation properties. A statistically significant correlation between recalcification time and passage of weather fronts was likewise established, confirming the previous findings of Caroli and Pichotka (see p. 319).

The *penetration of micro-organisms,* with their protein molecules and toxic substances, into the body tissues stimulates the production of antibodies and antitoxins, similar to the action of antigens (see p. 460). These antibodies may cause the coherence of bacteria or may dissolve them due to a substance known as *agglutinin.* Studies by Tokumitsu and others suggest that adrenaline, thyroid and parathyroid hormones affect the agglutinin content of immunized animals. The antibodies seem to have a stimulating effect on the *phagocytic cells* (see p. 284), which are able to absorb and destroy micro-organisms. As the functioning of the spleen can be affected meteorologically, specific weather conditions affecting the orthosympathetic nervous system may affect the resistance of the body to infectious diseases.

The fact that *leucocytes* also play an important part in the destruction of penetrating micro-organisms is well known. It was pointed out on p. 284 that both short-term and long-term seasonal changes in the leucocyte count are observed in healthy persons as a result of meteorological factors. It may be added that the seasonal changes in the protein spectrum of the blood serum and of the leucocytes occur before the seasonal changes in diet or other sociological habits take place. It is highly probable, therefore, that the observed changes in gamma-globulin are really due to changes in weather stress affecting the general resistance of the whole population.

The activity of leucocytes is affected by different exogenous factors: (*i*) With rising temperature (up to 38–40° C) the speed of amoebic movements (observed under a microscope) increases, the protoplama becomes less viscid, the granules in the leucotyte protoplasm move faster, the pseudopodia become broader. (*ii*) According to Hoff (*Fieber, unspezifische Abwehrvorgange, unspezifische Therapie*, Georg Thieme Verlag, Stuttgart, 1957), studies by various authors suggest that increased activity of the orthosympathetic nervous system activates the functions of the leucocytes, whereas a high parasympathetic tonus lowers the activity.Dietrich (in H. BRAUNSTEINER, *Physiologie und Physiopathologie der weissen Blutzellen*, Georg Thieme Verlag, Stuttgart, 1959) also concluded that disturbances in the functioning of the hormonal and autonomic nervous systems are reflected in the activity of the leucocytes. (*iii*) According to von Philipsborn[2457a] the leucocytes become more mobile and active during pregnancy, after loss of blood (over 300 cc), physical labour, electric shock, hot baths and after treatment with vitamins A, B and C and histamine. Cortisone has an opposite effect. (*iv*) According to Baudisch, leucocytic sticking (*i.e.* the property of leucocytes to stick to solid surfaces) is decreased by heparin and other factors affecting blood coagulation (see p. 286 and 318).

Studies by Wildführ[2499-2502] and Welcker indicate *changes in the anti-toxin content of the blood* at different seasons and after the passage of weather fronts (see p. 375).

The studies made by Zimmermann[961], briefly described, on p. 329, suggest a relationship between 17-KS level and general resistance. *All weather stress conditions causing a decrease in 17-KS level seem to lower the resistance.* Whether this is a direct causal relationship or an indirect one is not yet known. As pointed out on p. 328, weather conditions increasing the 17-KS level also increase adrenaline secretion, stimulation of the spleen and release of leucocytes in the blood stream. As a rule, an increase in albumin and decrease in globulin level of the blood gradually follow. A change in the weather (*e.g.* influx of warm air masses) may create a situation in which 17-KS and leucocyte levels are low, whereas the gamma globulin level has not yet increased. If, under these circumstances, one or more of the factors effecting the "local resistance" permitted the penetration of micro-organisms, the factors determining "general resistance" might not be able to destroy the invading micro-organisms. Zimmermann pointed out *(7th Int. Congr. for Microbiol., 1958)* that only *steroid hormones with anabolic properties* (*i.e.* constructive protein metabolism), *e.g.* certain androgenic hormones (see pp. 260 and 324), seem to increase the general resistance, whereas *corticosteroids* apparently act catabolically (destructive metabolism) and lower the resistance. He was able to demonstrate this experimentally in about 80 children suffering from various degrees of tuberculosis. During periods of aggravation the 17-KS level of the urine was low, that of the corticosteroids high. The former may drop to 54% of the normal level of healthy children, whereas during periods of improvement the 17-KS level may reach 88% of the normal value. A group of mice living on a protein-deficient diet (which lowers the 17-KS secretion, see p. 326) and infected with *Salmonella typhimurium* showed a similar consistent relationship, *i.e.* a considerably lowered 17-KS secretion during periods of decreased resistance and high levels during periods of great resistance (for further details see *Beitr. Klin. Tuberk.*, 117, 193–228 (1958).

As sudden cold or heat stress may cause a dysfunction of the thermoregulation system and, therefore, of the many physiological processes controlled by the hypothalamus, it is clear that *thermal stress could seriously affect the general resistance of the human body to infectious diseases.* An interesting analysis of this problem was given by Mills[2449]. Mills and Colvin continued the studies of A. Locke[2444b] at Pittsburgh (U.S.A.), who observed that resistance to infection was highest in those animals whose oxygen consumption was most sharply increased under the stress of body chilling. According to Locke, also in men, *those with most active combustion rates were least susceptible to cold.* Experiments by Colvin at the Lab. for Exp. Med. at Cincinnati (U.S.A.) demonstrated that mice, placed in two rooms and adapted for 3 weeks to temperatures respectively of 91° F (and 60% R.H.) and 65° F, showed striking differences in their ability to survive various types of artifically created infections. Although both groups were healthy before the infection and the average life span of the animals in the warm room was longer than that of the cold room, the animals in the warm room had less ability to resist infections, probably partly due to their lower combustion and energy level, partly because of a difference in development of the micro-organisms. Warm-room mice were killed with only 1/4 of the dose of a haemolytic streptococcus culture it takes to kill those of the cold room. The observation was confirmed by statistical studies on *acute appendicitis* in 25 American cities (Mills[3009a]). During summer heat waves the incidence was almost twice that during winter. Complications (perforation, spreading peritonitis, etc.), too, occurred more easily in summer. A study of 3179 histories of patients who died from *tuberculosis* near Cincinnati, in the same sanatorium, between 1909 and 1934 revealed a slower course and longer life span in those born in the North. White patients born in the North lived 22.3 months against those from the Gulf States 11.8 months. For negroes the figures were 16.8 and 9.4 months respectively. The same differences were found amongst European emigrants from the Mediterranean and N. European countries (Mills[2419]).* According to Mills, *acute nephritis* is also highest in the tropical moist regions.

This brief summary of the possible effect of weather and climate on the resistance of the body to infectious diseases is far from conclusive, but the facts observed so far appear to support the assumption that weather and climate must play an important part, not only in most epidemics of infectious diseases, but also in the local outbreak of such diseases.

2. *Influence of Weather and Climate on the Ease of Spread of Infectious Diseases*

In this section only the influence of weather and climate on the development and spread of micro-organisms will be discussed. The effect on the social habits of man, facilitating contact, had to be omitted for lack of space.

Influence of weather and climate on the development of micro-organisms and viruses

The study of the influence of weather and climate on micro-organisms

* It should be borne in mind that differences in immunity, as explained on p. 503, are also involved.

comprises two problems: (a) The possible effect on the virulence of these organisms and viruses and (b) on their development.

(1) *Possible influence of weather on the virulence of micro-organisms.* Neither the studies by Stallybrass (in 1931), nor of Webster (in 1946), Lebrun and Delaunay (in 1954) and Coburn *et al.* (in 1957) seem to confirm the assumption that the virulence of micro-organisms changes in different periods of the year. Webster[2457b] isolated bacteria from animals who died during an artifically created epidemic. The virulence of these bacteria did not apparently change during the year and was the same as that of the original group used for the epidemic. It should nevertheless be borne in mind that our techniques may not be sufficiently sensitive to demonstrate small changes in the production of toxic substances by a few bacteria only. However, so far the various studies suggest that, if changes do occur, they cannot be of great pathological significance.

(2) *Meteorological factors affecting the growth and development of micro-organisms.*

(*i*) *The influence of temperature, humidity, air movement and ultraviolet solar radiation* on the development of micro-organisms on the human skin was briefly reviewed on p. 512.

(*ii*) Krueger, Wesley Hicks and Beckett (p. 353) reported on *the effect of unipolar air ions* on micro-organisms and on the evaporation of droplets. The experiments were carried out at the Dept. of Bacteriology at the University of California, U.S.A. Staphylococci were suspended in small drops of distilled water and were exposed to unipolar air ions. Under conditions of clean air, it was found that increased ionization of the air caused a decreased survival rate of the micro-organisms and a slight increase in the rate of evaporation of the droplets. The lethal effect was found to be proportional to the number of ions reaching the surface of the droplets. As a result, the lethal effects will increase with decreasing size of the droplets and with increased movement of the droplets (air turbulence). On the other hand, contaminated air, with electrically charged particles, seems to have a shielding effect on the staphylococci and the survival rate increases.

(*iii*) *The influence of ultraviolet light* was briefly mentioned on p. 512. The lethal effect seems to be greatest if the relative humidity of the air is less than 60%. Whisler[2460a] and Wells[2457c] demonstrated this for bacteria in aerosols. Lidwell and Lowbury observed the same for dried bacteria on glass. On the other hand, the same authors noticed that strepto- and staphylococci in dust are more resistant in a dry atmosphere. Work by Buchbinder *et al.*[2436b] showed that ordinary daylight, even after passing through windowpane, also has a lethal effect on streptococci in dust with a

36% R.H. of the air. According to Edward (*Lancet*, 644, 1941) light also has a lethal effect on the influenza-A virus (Strain PR 8). The influence of the combined effect of light and humidity was recently demonstrated by Beebe and Pirsch[2427b] on the survival of *Pasteurella pestis and P. tularensis* (two species of a genus of Schizomycetes, the former causing bubonic and pneumonic plague in man, the latter causing tularaemia, *i.e.* a disease of rabbits and other rodents resembling plague). Again it was found that a 60% R.H. is a critical level. Bancroft and Pound[2427a] observed an increased concentration of viruses in plants four days after artificial infection of the leaves, with increase in daylenghth and intensity of the light radiation. The attainment of a certain maximum was followed by diminution. Diffuse light radiating for long periods caused a greater increase than strong light during a short period.

(*iv*) The *direct influence of temperature and humidity on the survival of air-borne micro-organisms* was studied recently by Hemmes at the Institute of Hygiene at the University of Utrecht (*The Survival of Air-borne Micro-organisms*, Thesis, Utrecht, 1959). The influence of humidity on the survival rate of a number of organisms (bacteriophage T_5, influenza virus PR8, Streptococci, Staphylococci and Neisseria species, etc) was determined at 10°, 20° and 30° C. The following results were obtained:

(α) Gram-negative micro-organisms generally have a higher death rate than gram-positive organisms. The gram-negative organisms die more rapidly at lower humidities. (β) Gram-positive micro-organisms and the influenza virus die more rapidly at high relative humidity of the environment. (γ) The death rate for both groups of organisms is maximal at a specific relative humidity or within a certain humidity range. This suggests that the conditions causing death depend on a critical water content of the organism. (δ) The death rates increase by a factor of 2 to 4 per 10 degrees of temperature rise (at least between 10 and 30° C). (ε) With reduced oxygen vapour pressure a reduction of death rate is observed. (ζ) Pathological micro-organisms can be classified into 2 groups, *viz.* organisms causing *summer diseases*, death rate being low at high R.H. (because the R.H. indoors is usually higher in summer than in winter); organisms causing *winter diseases*, death rate being low at low R.H. In the Tropics the so-called summer diseases occur in the wet season, the winter diseases in the dry season.

Hemmes pointed out that if no positive correlation exists between the morbidity of an air-borne infectious disease and temperature and humidity, the infection is very probably not due to the spread of infected droplets but to dust or other factors. Although the plant viruses are usually simpler in structure than the animal and human viruses, it is interesting to note that, according to Bancroft and Pound[2427a], the *virus concentration in plants* varies with different temperatures. It increases with rising environmental temperature and with the plant's rate of growth till a certain maximum is reached, after which the concentration decreases. Similar studies in relation to animals and man are recommended for future research.

(*v*) The *possible influence of meteorologically determined fluctuations in atmospheric pressure and infra-red radiation* is suggested by Bortels' experiments[2429-2432]. Daily studies by Bortels at the Bacteriological Institute of Berlin showed considerable differences in rate of growth of the same type of bacteria, despite the constancy of the growing medium. It was noted that in the Berlin area the growth of azo-bacteria increased more rapidly during periods of high atmospheric pressure than during periods of low pressure. Other micro-organisms as well displayed similar fluctuations. As these changes occurred notwithstanding constancy of temperature, humidity and light of the immediate environment of the growing medium and as thin metal sheets of aluminum, copper or lead affected the rate of growth, Bortels is inclined to believe that these changes are due to an unknown "weather radiation". He referred to Piccardi's observations (see p. 151). We should not forget, however, that in these experiments neither atmospheric pressure (which may affect the escape of gases from the growing medium) nor the infra-red radiation of the floor or walls of the room were always the same (see p. 37). It should be borne in mind that, although a thermostat keeps an air space on the whole at roughly the same temperature, considerable fluctuations in turbulence of the air surrounding the thermostat may cause greater heat drainage at certain times and therefore minor temperature fluctuations in the growing medium. In this connection we should like to refer to the experiments of Düll and Findeisen (see p. 589). Whatever the actual cause may be, the fact that the weather, even under apparently well-controlled conditions, is a potent factor acting on the growth of micro-organisms suggests that subtle changes in the meteorological environment are bound to affect the growth of pathological micro-organisms generally and aerobic micro-organisms in particular.

Influence of weather and climate on the spread of micro-organisms and viruses

Various studies have been made on the spread of micro-organisms in the air in relation to specific microclimatic conditions, *e.g.* in class-rooms or buildings.

As far back as 1887, Carnelly, Haldane and Anderson [*Phil. Trans. Roy. Soc. London, Ser. B, 178,* 61 (1877)] compared the number of micro-organisms settling on agar plates in the poorer parts of Dundee with the mortality from respiratory diseases. They found higher mortalities and seven times more micro-organisms of all kinds in one-roomed than in four-roomed houses. Flügge [*Z. Hyg. Infektionskrankh.,* 25, 179 (1897)] showed that infected droplets emitted from the nose and throat of a patient, by speaking or coughing, had a range of about one metre only.

On the other hand, Wells[2458-2461], using more efficient sampling methods, showed conclusively that micro-organisms can be recovered from the air at considerable distances from the human source. After the micro-organisms are projected from the mouth in droplets of moisture, which become lighter as the moisture evaporates, they are carried away on air currents over large distances in rooms or buildings. Only the large droplets fall down within a metre of the source. Similar studies were carried out by Reid[2449b], Williams and Lidwell for the Air Hygiene Committee of the Medical Research Council in London in 1954. The number of *Streptococcus salivarius* was determined from selective air samples of class-rooms in schools, and the general flora with a non-selective serum agar. Both were compared with epidemics of measles and colds in these schools. It was found that the most talkative classes had the highest streptococcus counts. It is also very likely that widespread aerial dissemination of infective droplets by air currents is important in the spread of these infectious diseases.

Studies by Kalra and Chand[2440, 2441] in 1956 at the Armed Forces Medical College, Poona (India), suggested that the maximum number of micro-organisms occur in the open air, but very few haemolytic (*i.e.* destructive for the blood) cocci; in buildings, with reduced direct ventilation, the total number of bacteria decreased but the percentage of haemolytic cocci increased.

Micro-organisms may first reach the floor of rooms or buildings. After drying up (the speed of which process depends on the humidity of the environment) and if protected from destruction, they may become air-borne, together with other dust particles, as a result of air movements (see p. 110) which are usually related to meteorological conditions outside the building (see p. 82). This aeroplankton may penetrate the nasal cavity or mouth of a person and re-become virulent with rising temperature and humidity.

The influence of weather and climate on the spread of micro-organisms may be *indirect* by its effect on certain insects (flies, mosquitoes, etc.) which are the actual carriers of the pathogenic micro-organisms. This problem will be disucssed more fully by Haufe on p. 688. In this connection the studies on the influence of *differences in smell of the human body* on the attraction of malaria mosquitoes are most instructive. Studies by Muirhead-Thompson[2448a] in Jamaica and Trinidad revealed that babies are bitten more than adults, males more than females. Thomas[2455a] observed the same in Sierra-Leone (Africa) for *Anopheles gambiae*. Smart and Brown[2453a] observed that among persons of the same race and skin colour, *Aedes aegypti* (transmitting the organisms of yellow fever and dengue) is most attracted by the person with the highest skin temperature. A heated or cooled hand is less attractive to mosquitoes than the normal hand. Dark skins or cloths attract mosquitoes most (according to Gjullin the attraction decreases from black through red, brown, yellow to white).

Bronwer (Thesis, Leiden, 1958) was able to eliminate various possible causes of the above observations by carefully planned laboratory studies, using an air-current olfactometer. The differences in attraction are not due to differences in radiation or movement of the subject. Nor are differences in temperature and humidity primarily responsible. It was found that the main cause is the *difference in smell*, which is due to different concentrations of propionic acid, isobutyric acid and other fatty acids in the sweat of the skin.

It is evident that all meteorological factors affecting the composition and the amount of sweat on the skin (see pp. 216 and 512, its evaporation and spread in the air are likely to play an important part in the spread of malaria, yellow fever and other similar diseases. It is also due to the local microclimate near houses that, in the Tropics, the majority of mosquitoes are found on the lee side of huts in which the native population is living (*Die Umschau*, June 1958).

3. Influence of Weather and Climate on Angina tonsillaris, the Common Cold, Diphtheria and Scarlet Fever, Influenza, Poliomyelitis anterior acuta, Epidemic Cerebrospinal Meningitis and Whooping Cough[2462-2547]

The clinical symptoms, causative agents and yearly period of maximal development of a number of important infectious diseases are summarized in Table 38.

Classification of meteorotropic infectious diseases

According to Stallybrass, Winkler, Hemmes and others, the meteorotropic infectious diseases can be classified into three groups: (*i*) *Summer diseases*: cholera, typhoid fever, poliomyelitis and, in Germany, bacillary dysentery, with increase in incidence from May to September. In the Tropics, the maximum incidence is during the rainy seasons and in the humid areas. (*ii*) *Autumn diseases*: streptococci infections of W. Europe, scarlatina and diphtheria, with increase in incidence from August to November. (*iii*) *Winter diseases*: the common cold, influenza, lobar pneumonia, epidemic cerebrospinal meningitis and smallpox (variola) increase from September to March. In the Tropics, the maximum incidence is in the dry season and in dry areas.

Many epidemiologists are inclined to account for some of the seasonal fluctuations by differences in humidity and temperature, as suggested by survival experiments (see p. 519)

The summer diseases occur during periods when environmental temperature and humidity are high; the winter diseases occur when the outside temperature is low and the humidity high, the humidity indoors, however, being low. According to experiments performed by Hemmes (see p. 519), the influenza virus dies more rapidly at high relative humidity. The virus is, therefore, more readily transferred by infected droplets or dust in dry rooms in winter. However, no simple relationships are found for the autumn diseases. This supports our previous statement that the meteorologically induced seasonal fluctuations of the general resistance of the population may play a more important part in the epidemiology of diseases than is generally recognized.

More detailed biometeorological studies have been carried out for a number of infectious diseases.

Angina tonsillaris (quinsy)[2462 2469]

Herbst[2466] reported on the relationship between the incidence of tonsillitis at Graz (Austria) and periods of sudden falll in temperature due to the influx of cold air masses and cold fronts. Similar observations were described by Uffenorde and Gilse[2469] and Greifenstem[2465]. According to the latter, post-operative tonsillitis is particularly common after the influx of polar air.

The first accurate statistical study was carried out in 1941 by de Rudder (in co-operation with the meteorologist Linke) in Frankfurt (Germany) at the University Paediatric Clinic. With the N-method (see p. 176) the meteorotropic significance of 64 cases of angina tonsillaris were analysed in relation to weather fronts. Although a maximum occurred on the N-day, it was not highly significant. A similar analysis by Koerbel[2467] in Vienna produced only a 96% significance. However, combination of the data of both studies established a statistically significant correlation. De Rudder pointed out that the influence of weather on streptococci development is supported by the observations of Sundermann and Baufeld[2468] at the Medical Clinic of Jena University (Germany). They showed that, in the period between 1944 and 1948, the daily number of streptococci on the tonsils of four different groups, each composed of 50 people who had no contact whatsoever, displayed synchronous changes which can only be explained by environmental changes occurring regionally. So far, the only regional factor which could be involved seems to be the daily changes in weather, the influence being either direct or indirect (*e.g.*, due to daily fluctuations in contact facilities).

TABLE 38

CLINICAL SYMPTOMS, CAUSATIVE AGENTS AND YEARLY PERIOD OF MAXIMAL DEVELOPMENT OF A NUMBER OF IMPORTANT INFECTIOUS DISEASES

Infectious disease	*Clinical symptoms*	*Causative agents*	*Yearly period of maximal development*
Angina tonsillaris (quinsy)	Acute inflammation of one or both tonsils and of the surrounding tissue, causing fever, soar throat and difficulty with swallowing	Different micro-organisms, particularly haemolytic streptococci	Increasing after sudden influx of cold air (studies by Häupler and Brezowski)
Asiatic cholera	Acute inflammation of the intestines, causing superficial sloughing necrosis of the epithelial lining of the gut, leading to violent diarrhoea and considerable fluid losses. Incubation period: 1–6 days	*Vibrio comma*, a gram-negative rod-shaped, motile species of the genus schizomycetes	Rare in Europe but max. in Aug. In India and surrounding countries common in hot humid tropics except during Jan.–Febr. if in these areas the temperature drops considerably
Common cold	Catarrhal inflammation of the upper respiratory tract with acute profuse discharge from the mucous membrane of the nose. Incubation period: 24 h up to few days	*Virus Tarpeia premens* (probably 20–50 m μ)	According to Simpson, minimum in September, max. in February–March (in N. hemisphere). In Holland and England increase in incidence with falling temperature and rise in humidity (studies by Van Loghem, Reid and Simpson)
Diphtheria (and croup)	Acute formation of false membranes in throat and nose causing dyspnoe or complete closure of the pharynx. Incubation period: 2–4 days	*Coryne bacterium diphtheriae*, a rod-shaped gram-positive bacteria	In W. Europe Nov.–beginning of Dec., beginning in Aug., max. in Nov.–beginning of Dec. but still high till February
Dysentery	Inflammation of the large intestine, with evacuation of liquid and bloody stools and painful straining at stool. Incubation period: 1–4 days	*Entamoeba histolytica* (causing amoebic or trop. dys.) or *Shigella dysenteriae*, rod shaped gram-negative bac. (causing bacillary dysentery)	B. dys. in Germany max. in summer, in Gr. Britain Febr.–April, in the Tropics in the rainy season
Influenza	Distressing fever, depression, acute catarrhal inflammation of nose, larynx and bronchi, neuralgic and muscular pains, gastrointestinal disorders	*Filtrable virus* of various strains and *Haemophilus influenzae*, rod-shaped, gram-negative bact.	In colder parts of N. hemisphere max. in Dec.–Febr. (virus does not disappear in summer); in S. hemisphere June–August. In 1918 in France and England epidemic related to dry cold periods. In 1956 in the

pneumonia	formation of an exudate in the interstitial and cellular portions of the lung, high fever	*Klebsiella pneumoniae* (gram neg. bact.) or *Virus influenzae*	in Tropical Africa max. during dry season. High mortality if temperature during preceding week has been lower (studies by Young, Payling and Wright)
Meningitis cerebrospinalis epidemica	Acute inflammation of the membranes of the brain or spinal cord marked by high fever, strong headaches, stiffness of neck, disturbance of consciousness	*Neisseria meningitidis*, gram-negative cocci	In W. Europe beginning in autumn, high in December–April; in the U.S.A. max. in Febr.–March, in Tropical W. Africa max. in dry season in dry areas
Poliomyelitis anterior acuta	Inflammation of gray substance of spinal cord, marked by fever, paralysis and muscular atrophy. Incubation period: 1–4 weeks	*Virus legio debilitans*	In N. hemisphere min. in March and beginning of April, inceasing in April with max. in Aug.–Sept; in S. hemisphere min. in Sept.–Oct. Near the aequator, no seasonal fluctuations
Scarlet fever (scarlatina)	Infectious exanthematous disease, accompanied by very high fever, headache, inflammation of throat, vomitting, red rash, dark red tongue. Incubation period: 3–5 days	*Streptococcus scarlatinae*	In W. Europe beginning in Aug., max. end Oct.–beginning of Nov., the end in December In New York and Chicago max. in Febr.–March. In northern U.S.A. incidence three times Southern part, in the Tropics rare. Scarlatina and other streptococci infections usually highest during years with low humidity (studies by Wood and Coburn)
Typhus (exanthematicus)	Petechial eruption, high temperature and extreme exhaustion. Incubation period: 1–2 weeks	*Rickettsia prowazeki* transmitted by tissue cells of body lice, ticks, mites or the flea *Xenopsylla cheopis*	If transmitted by ticks, peak of infection May–July (in N.Europe), coinciding with peak of breeding season among ticks
Typhoid fever (typhus abdominalis)	Inflammation of the mucosa of the gut with bleeding, high fever, etc. Incubation period: 1–3 weeks	*Salmonella typhosa*, gram-negative bacteria	In W. Europe increasing from May till September, followed by rapid decrease from middle of Sept. In Java max. in wet season
Variola (smallpox)	Vomiting, fever, papular exanthema leading to pustular eruptions. Incubation period: 7–21 days	*Virus borreliota variolae*	In N. hemisphere beginning in August, max. in March, In India and Ghana max. in dry periods
Pertussis (whooping cough)	Infectious disease characterized by coryza (discharge of mucous membrane of the nose), bronchitis, violent spasmodic cough and "hougling" inspiration. Incubation period: 7–10 days	*Haemophilus pertussis* (gram-negative bacteria)	No particular period for all countries in N. hemisphere and different for different years, but often in spring and autumn

The common cold[2470–2485]

On p. 513 we briefly described the observations of Hill and Article during the war, which have been erroneously interpreted as an indication that temperature has little effect on the common cold. On the other hand, Townsend and Sydenstricker, studying 11000 students and 775 families all over the U.S.A., for the U.S. Public Health Service in 1923 and 1924, found that waves of the common cold more or less synchronised everywhere (in October the incidence was 30/100 reporters, in December 14, in January 25), which suggests the influence of regional meteorological factors.

Between September 1925 and June 1926 similar studies were carried out by van Loghem[2531]. He studied the influence of meteorological factors on the respiratory diseases of 7000 volunteers in the Netherlands, comprising 1523 families and 335 individuals. The following results were obtained: (*i*) The increase and decrease in incidence take place synchronously all over the country. (*ii*) The periods of increase and decrease in the incidence coincided with periods of fall and rise in temperature respectively. (*iii*) No difference in incidence was found between small or large families, from which it may be inferred that the contact factor is of minor importance. (*iv*) During the period of November to May (especially Nov.–Jan.) the common cold curve runs parallel to the curve for bronchitis-pneumonia mortality; the rise, however, begins earlier in the curve of the common cold. Van Loghem assumes that the cold is due to an infection after an initial, meteorologically determined, *disturbance of the thermoregulation of the population*. The significance of the thermoregulation centre was discussed on p. 516.

Sargent[2450–2453] studied the day-to-day course of the weather and of the incidence of respiratory infections (coryza, pharyngitis, laryngitis, bronchitis, tonsillitis and pneumonia) at the Philips Exeter Academy in Exeter (U.S.A.) from Sept. 1935 to June 1938. For this study 700 students, varying in age from 14 to 19, were used. The following observations were made: (*i*) Increase in common cold incidence was associated with cold-front passages or the following high-barometric pressure crest, depending on whether the incubation period took a few hours or days. (*ii*) The summation of consecutive polar air influxes, in particular, would suddenly increase the incidence of common cold.

Petersen and Sargent[2452] have pointed out that, as body habitus is closely related to our heat-regulating mechanism (see also pp. 230 and 673) it is possible that a relationship may exist between *common cold incidence and body habitus*. In an endeavour to verify this proposition, 93 boys at the Philips Exeter Academy were studied from 1935 to 1939. Three types of body-build were distinguished, based upon the Baldwin-Wood Tables the height-weight relation being determined by the formula

$$K = \frac{\left(\frac{H}{10}\right)^{2.5}}{0.92\ W}$$

Boys with $K > 1.10$ were classified as *leptosome* (tall slender type), having a large body surface in proportion to body weight; $K < 0.90$ were classified as *pyknic* (short, broad type), having a small body surface in proportion to body weight; $K = 0.90 - 1.10$ were called *normal*. It was found that in autumn pyknics have the highest rates, in spring the leptosomes; in winter usually the pyknics prevail.

Space prevents us from discussing many other interesting studies in this field. The studies of Reid[2449b], will be reviewed briefly. Williams and Reid studied the occurrence and spread of the common cold in London offices of the General Post office in 1953. The sudden autumnal fall in outside temperature coincided with a sharp increase in common colds. However, it also coincided with the shutting of windows and a steep increase of *Streptococcus salivarius*. Shutting windows also facilitates the spread of close-range droplet spray by carriers of an infection. Still further studies revealed that actually the sudden cold and low endemic level of infection during summer are mainly responsible for the epidemic. Some of the facts supporting this view are the higher incidence among the less adequately clad children; the lower incidence in class-rooms which are kept at higher temperatures despite a high streptococcus level, etc. The influence of fall in temperature on children is also shown by Wright's studies[2461a]. They showed that the weekly mortality-rate from bronchopneumonia in children under 2 years of age was strikingly *correlated with a fall in temperature two weeks before*.

Diphtheria[2483–2502] and scarlet fever[2536–2511]

In W. Europe both diphtheria and scarlet fever have a rather similar seasonal development (see Table 38), *i.e.* high incidence in the early winter. However, the incidence of scarlet fever wanes rapidly in December and January, whereas that of diphtheria remains high till February. In the U.S.A., diphtheria has a sharp peak in December, falling off rapidly to January, whereas scarlet fever has a maximum incidence in February (period 1920–1929). In the S. hemisphere the maximum is reached 6 months later, *i.e.* in August.

The differences in the period of maximum incidence, the fact that the incidence during summer in the school period and during the holidays is the same and other similar observations suggest, according to De Rudder [6, p. 235], that the winter peak is probably not due to increased contact facilities.

It seems more likely that seasonal differences in resistance are involved. This assumption is supported by Gallenkamp's observation[2492] that the amplitude of the diphtheria peak in winter increases with the age group of the children, suggesting that differences in resistance play an important part in these diseases. This view is also supported by Wildführ's observation (see p. 375) that the diphtheria antitoxin level of the blood in winter is 2 to 3 times lower than in summer. Gundel's assumption that the high peak in December is due to many respiratory infections is an unlikely one because the respiratory infection peak occurs in February. Years with an exceptionally high incidence of diphtheria are not necessarily characterized by a high incidence of common colds, etc.

According to Wildführ, neither cold stress nor vitamins affect the antitoxin level of the blood serum. De Rudder [6, p. 240] is therefore inclined to assume that the *decrease in ultraviolet radiation in winter* is mainly responsible for the decreased resistance. The low incidence of diphtheria and scarlet fever in sunny tropical areas lends support to this view, but the fact that *Corynebacterium diphtheriae* (see Table 38) is a gram-positive bacterium which dies more rapidly at high relative humidity (see p. 519) may be another causal factor. Considerably more research is required before the exact cause of the winter peak can be explained.

Influenza[2503–2519]

Influenza is another interesting infectious disease in the N. hemisphere with maximum development in winter (see Table 38) and a similar peak in the S. hemisphere six months later. In W. Europe it usually reaches a maximum at the end of January and the beginning of February.

During the period of 1954–1958 the curve representing the weekly percentages of males reported to be suffering from influenza in the Netherlands between January and March (based on 300,000 males working in 300 factories) is roughly in inverse ratio to the curve of the average weekly temperatures, *i.e.* the weekly morbidity curve is rising when the temperature curve is falling and *vice versa*.

Apart from the yearly pseudo-seasonal peak, serious *pandemics* (*i.e.* widespread epidemics) have occurred occasionally, *e.g.*, in 1889–1890, 1918–1919 (which is reported to have killed 15,000,000 people) and in 1957. This most recent epidemic came on gradually in the Netherlands in the middle of August, spread rapidly at the beginning of September and reached a maximum from the middle of September to the first part of October, depending on the district. In many respects 1957 was an abnormal meteorological year in the Netherlands. Except for May, August and September, the average monthly temperatures of the whole year were above normal, being as much as twice the normal in January and February. June and the first week of July were exceptionally hot. From the middle of August till the end of September the temperatures suddenly dropped to below average and the amount and duration of the rainfall were almost twice the normal, the total rainfall in September exceeding the highest on record in the last 100 years. As a result the hours of sunshine were far below normal (89 hours in September against 148 normally). Although 1957 was a very warm year, except in April, June and December, all months had a considerable shortage of sun hours, giving a total shortage of about 100 sun hours for the year. It was also a year in which there was a large percentage of healthy blood donors with high blood sedimentation rates (from 10th May till the end of October) and with low haemoglobin values (see p. 315 and 318).

Although it is difficult to predict the exact physiological effects of this abnormal meteorological year, the data summarized on pp. 471–473, tend to corroborate the assumption that the weather conditions must have affected the general resistance of the whole population considerably. The period of sudden cold stress and considerable cooling (due to excessive rain and many storms) in August and September, after the population had become acclimatized to warm weather for almost seven months in succession, must have caused a considerable disturbance of its thermoregulating mechanism. The lack of sunshine, particularly during that period of the year (May–September) when, in these parts, we normally have the maximum of it, affects the hormonal functions (p. 347) and resistance to infections (p. 511) and may have further lowered the general resistance. The fact that the epidemic actually started in the middle of August and increased rapidly in September, although the virus had already been active in the preceding months, suggests that this general lowering of the resistance of the population may have been more important than the increased risk of contagion through contact after the summer holidays, which has always been considered the main cause of the September-October peak.

A detailed biometeorological analysis of the whole influenza epidemic in the Netherlands by Tromp makes it look as though important changes in general morbidity were related to sudden weather changes, such as a sudden steep drop in barometric pressure accompanied by passages of cold fronts, influx of cold polar air, strong winds, heavy rain, hail or thunderstorms followed by a rapid fall in temperature. Apparently, a sudden influx of warm fronts and warm air arrested an epidemic in some particular region if the incidence had already mounted high there. Nevertheless, much more research is required to clarify the exact significance of weather in relation to the development of influenza epidemics.

Poliomyelitis anterior acuta[2520-2535]

Apart from the study of the cause of the seasonal peak of this disease many scientists have devoted a considerable amount of research to the problem of the possible influence of weather on the outbreak and development of poliomyelitis. Only some of the theories put forward will be briefly reviewed here.

Van Loghem[2532, 2533] has pointed out that, in 22 countries outside the Tropics, poliomyelitis has a pronounced seasonal peak (see Table 38), with a difference of six months between the N. and S. hemispheres.

A similar study was carried out in 1960 for 12 countries in different parts of the world located near the equator, where seasonal climatic differences are very small or absent altogether. In these countries no seasonal peak in the incidence of polio is seen to occur.

In this connection de Rudder's statement[6, p. 180] that epidemics in Scandinavia are usually more violent than in Germany, these again more violent than in Italy and, finally, that there are relatively few serious cases in the Tropics, is interesting.

Van Loghem pointed out that the morbidity curves of the polio epidemic in 1952 in the Netherlands, Belgium, various Rhine provinces of Germany and similar curves for 5 epidemics in the U.S.A., between 1942 and 1946, have a striking resemblance. In approximately the 18th week of each epidemic year the curves begin to rise and reach a sharp maximum during the 32nd–37th week, dropping to the zero level again around the 50th week. This observation and the fact that epidemics are liable to occur during either warm dry or cold wet summers argue against any significant implication of the weather conditions during and just before the epidemic in this seasonal phenomenon. These facts and the six-month time lag between the peaks in the N. and S. hemispheres suggest that, either the development and spread of the virus, or the human resistance of the population (or both) all over the world changes at a specific time of the year, irrespective of great differences in race, climate, food and social conditions in these different areas. This makes it reasonable to assume that an important astronomical climatic factor must be involved, such as changes in solar radiation, gradual yearly change in average monthly temperature and the like.

Whereas the maximum peak does not occur exactly at the same time in different countries, the lowest point is fairly simultaneous. It has also been noticed by van Loghem and others that, during the smaller seasonal epidemics, the sudden increase starts in many areas at the same time and there is no gradual spread from one city to another. This indicates that gradual spreading of the infection through increased contact, as in the case of influenza, does not play an important part in this disease. It seems that the permanent symbiotic equilibrium between the population and the virus is suddenly disturbed by a regional exogenous factor at a certain time of the year and the more violent, the greater the distance of the country from the equator. Studies by Fox in Louisiana have shown an increased secretion of the polio virus by virus carriers during the polio season, causing an increased immunization but also an increase in the number of new cases.

Although, generally speaking, single meteorological factors do not appear to affect the development of the seasonal polio peak, the following studies suggest that weather may play a certain part in this complex disease.

In 1935 Petersen and Benell[2528–2529] observed in Chicago that the preparalytic stage usually started after the passage of a cold front, the paralytic stage being precipitated by a second cold front. It emerged from a statistical study that the highest incidence of polio occurs during periods of strong cooling effects, the minimum being during warm periods.

De Rudder[6, p. 75] studied this association with cold fronts for the city of New York. Using the N-method (p. 176), he found a statistically significant correlation, but a similar analysis of 167 cases in Frankfurt (Germany) in 1938–1939 did not confirm previous observations. However, it may be that there was a considerable difference in front activity in the two cases. Thus, for instance, not every passage of a cold front is accompanied by considerable cooling effects.

Armstrong[2529–2523], formerly medical Director of the Microbiological Institute of the National Institute of Health, Bethesda, U.S.A. collected extensive evidence that certain meteorological conditions seem to lower the local resistance against the poliomyelitis virus in the respiratory tract. He pointed out that when atmospheric air is breathed it is found upon expiration to be uniformly warmed to about 90° F with R.H. of about 90%, *i.e.* a moisture content of approximately 35 g/m^3. The moisture increase has come from the respiratory passages. Cool dry air in winter will have a drying effect on the mucous membrane. However, the higher the relative humidity of atmospheric air the less this drying effect will be. Armstrong converted the observed daily relative humidities to temperatures of 90° F. A striking similarity was observed between the curve representing average weekly adjusted relative humidities and the incidence curve of cases of poliomyelitis during periods of polio epidemics in the U.S.A. The following observations were made.

(*i*) Poliomyelitis incidence began to rise when the adjusted relative humidities rose above 27-28% and the incidence fell rapidly as soon as the humidity dropped below this value. (*ii*) Calculations by Winslow, *et al.*[2535a] on the relationship between vapour pressure and marked drying of the respiratory mucous membranes indicate that drying occurs under the following conditions: temp. 53° F, R.H. 90% or less; 60° F/77% or less; 70° F/54% or less; 80° F/39% or less; 90° F/28% or less. (*iii*) During the 1950 epidemic in Virginia (U.S.A.) there were 4 high relative humidity peaks (above 28%). In each instance these peaks were followed 3 weeks later by a high polio peak. The highest polio peak coincided with the highest humidity peak. A similar striking correlation was found for the Denver epidemic in 1951. (*iv*) Membrane permeability increases with increased temperature (see p. 335), but only under certain moisture conditions. This could explain why only above 28% adjusted R.H. at 90° F the polio virus could penetrate more easily. Differences in membrane permeability (affected by the hormone secretion of the adrenal cortex) between different people may partly explain why in a certain environment only certain people are infected. (*v*) On p. 513 the possible relationship between humidity of nasal mucous membranes, antibody production against poliomyelitis and concentration through drying have been discussed.

These various observations seem to support Armstrong's hypothesis of the meteorotropic cause of poliomyelitis epidemics.

On the evidence of studies by Gear[2526a] in S. Africa, despite the occurrence of epidemics both during dry and wet periods, the main epidemics in this arid country occurred in years of excessive rainfall. If the yearly seasonal rains are late, the polio epidemic is also late. During these epidemics, apparently far more Europeans than indigenous Bantus are struck down by the disease, which is a reversal of the pattern with many other infectious diseases. It is also interesting to note that the examination of sewage for virus in Johannesburg revealed the absence of the virus during inter-epidemic periods. This confirms the conclusions arrived at by Fox. The fact that an epidemic of poliomyelitis apparently does not spread rapidly by increased contact among the population suggests that a seasonal change in general and local resistance may be a principal factor in this disease.

We have seen that asthma patients show a similar seasonal curve, with low values in winter, slowly increasing in spring and abruptly increasing in July, August and September.

A number of important changes in the physico-chemical state of the blood and of the functioning of the endocrinal and autonomic nervous systems during winter and summer were reviewed on p. 471. Some other seasonal physiological changes are set forth in Table 39 (p. 575). This whole group of regular seasonal changes (particularly important in children), due to the yearly changes in temperature, solar radiation, air turbulence, etc., should be studied in detail in relation to the problem of poliomyelitis in its entirety. It might furnish a clue to the cause of, and possible preventive measures against, the occurrence of poliomyelitis epidemics in summer.

Epidemic cerebrospinal meningitis[2436a]

The characteristic seasonal development of this disease is set out in Table 38. Usually a maximum is observed in February–March. Brezowsky and Menger[2436a] studied the possible meteorotropic character of this disease from 1952 to 1957, using clinical material from Munich, Mainz, Bremen and Norderney (Germany). The weather-phase method of Ungeheuer was used for the correlation studies (see p. 24). In Bremen and Mainz a mathematically significant statistical correlation was established between the *occurrence of meningitis and the influx of warm humid air masses* (weather-phase Wph4). Similar relationships were previously found by Daubert and Kuhnke in Tübingen and Hamburg in relation to various infectious fevers. In Munich, where the difference between these types of weather is less pronounced, no significant correlation could be established. This fact might account for the differences in degree of meteorotropism observed by workers in different countries.

Whooping cough (pertussis)[2542-2547]

Of the various meteorotropic infectious diseases, pertussis is particularly important because remarkable results have been obtained by subjecting patients suffering from whooping cough to high altitude (oxygen) stress (see p. 293).

Kettner (in 1927) Goering (in 1929), Nagel (in 1935), Jongbloed (in 1938), Morhardt (in 1939), Rober (in 1939), Capitummino (in 1940), Lauerner and Maeder (in 1942) and others have stressed the therapeutic effect of flights in non-pressurised aeroplanes on patients suffering from whooping cough. On account of the possible physiological mechanisms involved, several physicians applied a climatic (low-pressure) chamber treatment (see later p. 641). In 1953, Krieger[2547] studied the effect of this high altitude (low pressure) treatment on 726 children suffering from whooping cough. The therapeutic effects were compared with the results previously obtained by Bamberger and Menke[2541a] with 100 untreated children.

The treated children were placed in a climatic chamber, where, in about seven minutes, they were raised to an artificial altitude of 4000 m (450 mm Hg). They remained at this "altitude" for 30 minutes, after which the pressure was raised again. In approximately 15 minutes the normal sea-level pressure was regained. The treatment took place every other day, three times in succession. The following observations were made: (*i*) After three weeks, the treated children suffered far fewer attacks of coughing than those still assailing the untreated children at the end of seven weeks. (*ii*) Shortly after the beginning of the treatment, the attacks grew worse, but this was quickly followed by an improvement; as a rule, the sharper this initial exacerbation was, the better were the results after further treatment. (*iii*) The best results were obtained if the treatment started two weeks after the onset of the disease and about 84% of the treated children were cured; results were less favourable if the treatment started either after the first or after the 3rd–4th week. (*iv*) The treatment produced an improvement in the general health of the children, whose appetite increased; very serious attacks virtually ceased. (*v*) As the same high curative effect was observed even in very young children (less than 1 year of age), the influence of suggestion can be ruled out.

The encouraging results obtained with whooping cough and bronchitis suggest that perhaps other infectious respiratory diseases may also benefit by climatic chamber treatment, particularly if combined with aerosol treatment.

Subsect. G. MENTAL DISEASES[2548–2684]

1. *Importance of Biometeorological Studies*

A considerable number of studies have been devoted to the possible influence of weather and climate on mental processes*. This problem is a very old one but, in spite of the many publications which have appeared on the subject, most of the studies are inconclusive, either because the clinical material on which the conclusions were based was too small or untrustworthy, or because the meteorological data used were not sufficiently accurate.

Everbybody who has lived in the Tropics for a number of years knows from his own experience how difficult it is to do exacting mental work or to read serious books. Almost daily, after sudden drastic changes in the weather our psychological and emotional behaviour undergoes some change. This may be due in part to purely visual impressions which affect our mood, but

* (*i*) *Schizophrenia* or *dementia praecox* comprises a large, rather inhomogeneous group of psychoses characterized by disorientation, loss of contact with reality, splitting of the personality, etc. Several kinds of schizophrenia are distinguished: katatonia, hebephrenia and dementia paranoides. (*ii*) *Oligophrenia* (weak-mindedness) comprises three larger groups of mental diseases: debilitas mentis (persons suffering from mental deficiency, having difficulty in learning and in controlling themselves or managing their own affairs), imbecillitas (more serious form of mental debility, with 25–50 I.Q.) and idiocy (a severe mental deficiency, the person being incapable of guarding against common physical dangers, I.Q. less than 25). (*iii*) *Epilepsia*, a mental disease marked by seizures with convulsions and loss of consciousness. (*iv*) *Apoplexy*, sudden paralysis and coma from cerebral effusion (escape of fluid) or extravasation of blood into the brain tissues. (*v*) *Hemicrania* or *migraine*: one-sided headache.

the evidence of recent studies points to the occurrence of real physiological changes in our body which may well seriously affect our mental processes. These studies are more than merely academically interesting, as they may have a number of important social and scientific repercussions. *E.g.*,

(1) If certain *biometeorological relationships* are found, these may be helpful in the study of the physiological processes involved in the registration of environmental stimuli.

(2) In the case of *mental patients* they may suggest means of decreasing the restlessness and ill-temperedness of such patients (see p. 647).

(3) There appears to be some evidence that *schizophrenia and the incidence of mental deficiency in children* are somehow tied up with the month of birth, the season and prevailing weather. Below we give some facts from which this evidence was inferred.

(*i*) In 1957 Pasamanick (Director of the Research Division of the Columbus Psychiatric Institute at Columbus, Ohio) and Mrs. Knobloch[2682, 2683] traced the month of birth of mentally deficient children born between 1913 and 1948 and institutionalized in the Columbus State School (see p. 674). It was found that schizophrenics are born significantly more often in January, February and March as compared with the standard monthly birth distribution in the U.S.A. Since the third month after conception, being the period when the cerebral cortex of the unborn child is becoming organized, would be June, July, August for this group, any environmental factor in these months causing a foetal injury might affect intellectual functioning. According to these authors, very high temperatures during these months and decreased protein intake might be one of the causes of such a trauma. They also found that the number of mentally defectives born after very hot summers is greater than after cool summers (see further also p. 442).

(*ii*) The same authors were able to show that the number of abnormalities in pregnancy are significantly higher in January, February, March when compared with the summer months (July–Sept.).

(*iii*) De Sauvage Nolting[2658, 2675], psychiatrist at the Psychiatric Institute Den Dolder (the Netherlands), listed the dates of birth of 8000 schizophrenics in the Netherlands and 7000 in Great Britain. He found, after the normal seasonal birth-rate correction, that a mathematically significantly higher birth-rate occurred during February and March, a minimum in June and July. No connection with the month of birth was found for epileptics and other mental diseases. De Sauvage Nolting is inclined to account for this distribution by a shortage of vitamin C in winter, which would aggravate the genetically determined susceptibility to schizophrenia because the otherwise stimulating effect of vitamin C on the healing process of damaged tissues (*e.g.* of the uterine mucous membrane) would be considerably reduced in winter.

(*iv*) Studies by Blonsky[2680] in Moscow in 1929 suggest that the intelligence quotient of schoolchildren in the USSR was highest for children born in the period from January to July (particularly April) and lowest between July and December (minimum in October).

(*v*) McKeown[3331] of the Institute of Social Medicine in Birmingham stated that more anencephalics are born in Great Britain in the period October–March (maximum in December) than in the period April–September (minimum May).

It is evident that if these findings can be confirmed and the deeper physiological causes can be established, the social implications will have far-reaching humanitarian and financial consequences.

2. *Influence of Weather and Climate on Restlessness of Mental Patients (Schizophrenics, Oligophrenics and Epileptics)*

The first large-scale statistical study of the possible influence of weather and climate on the restlessness and ill-temper of mental patients was carried out in the Netherlands by Tromp[2676a], between November 1956 and June 1960, in close co-operation with seven psychiatric institutes and 21 phychiatrists attached to these institutes. The latter, assisted by the matrons, made a daily record of both the degree of motor and psychic restlessness and ill-temperedness of the same group of mental patients. It was not the absolute unrest or ill-temperedness that was recorded, but the degree above or below the normal level, a subjective interpretation which could only be made by the sister and psychiatrist. The observations were made daily for 4 periods of the day: 0–6, 7–12, 13–18, 19–24 h. Other details concerning medical treatment (drugs used, etc.) were entered on the same record sheet. Obviously, only the motor unrest (clearly shown by shouting, scolding, quarrelling, throwing objects and so forth) can be accurately recorded. The type of patients used comprised schizophrenics, oligophrenics and epileptics, both males and females and of different age groups. A fairly homogeneous group of female schizophrenics of the same age and same social background served for a final study. The diuresis of a group of male schizophrenics was studied in 1960. On the basis of these daily observations, the percentage of restless patients and degree of restlessness can be calculated for each day. These data were then plotted against the meteorological data in the biometeorological logs (see p. 163).

Observations were made on schizophrenia, oligophrenia and epilepsy.

Schizophrenia

(1) In the Netherlands a clear statistical relationship between weather, season and the restlessness of schizophrenics was observed mainly in female schizophrenics. Therefore, the best correlations are found, in a statistical study, if a homogeneous group of female schizophrenics is used. The average monthly percentage of restless patients, above the normal level, in the group observed varied between 2% and 16% of the patients, the daily percentages fluctuating between 7% and 43%.

(2) Usually the highest degree of unrest is observed during the *early winter months* (November, December and January), which is demonstrated by the high monthly percentages of restlessness during this period and by the high daily percentages, these being higher and occurring more frequently than during the other months of the year. The November and December figures may also be low in warm winters or if the winter starts very late.

In other words, restlessness is not a truly seasonal phenomenon. In some psychiatric institutes a secondary peak of unrest has been observed in the months of July and August of certain years.

(3) The following correlations were found between daily fluctuations in restlessness and changing weather conditions: (*i*) The *barometric curves* often show a remarkable relationship with the *restlessness curves*. They are often almost parallel or inverse to them. This indicates that barometric pressure as such is not responsible for the fluctuations in restlessness, but apparently the abrupt changes in general distribution of barometric pressure over W. Europe and the North Sea are biometeorological indicators of certain important meteorological changes affecting the restlessness of schizophrenics. (*ii*) Not only barometric pressure in itself, but none of the other single meteorological factors, such as wind speed, wind direction, humidity, passages of weather fronts, etc., seem to correlate consistently with the observed restlessness curves. (*iii*) The only correlation found so far is the relationship between *air mass and unrest*. As a general rule, the following conclusions would appear to be valid in the Netherlands at least.

(α) Influx of warm continental, tropical maritime, or warm maritime air, causing a gradual rise in temperature of the atmosphere, increases the unrest of the schizophrenics. (β) Influx of cold continental, cold polar or cold maritime air masses have a reverse effect. (γ) Cold front passages in a period of warm air mass flow over W. Europe cause a temporary decrease in restlessness during such a period of high restlessness; warm front passages during a period of cold air masses cause temporary increases in restlessness in a period of quietness. (δ) These various meteorological factors, affecting the restlessness of the patients, have, apparently, even greater effect if the specific air mass conditions occur during periods of very strong atmospheric disturbances, such as very active deep depressions moving over the country, often accompanied by strong winds, heavy rain, hail, snow or severe thunderstorms.

(*iv*) Extreme temperature conditions may have an effect opposite to that mentioned above; *i.e.* very high temperatures during heat waves (as observed in 1957) may alleviate the general restlessness of schizophrenics. (*v*) Unpleasant weather conditions, such as heavy rainfall, snowstorms, lightning and the like do not affect the restlessness curves, unless they occur together with other meteorological conditions, as explained above sub. (*iii*). (*vi*) The amplitude of the restlessness fluctuations depends both on the factors mentioned sub. (*iii*) and on a pseudo-seasonal factor. The influence of the influx of cold and warm air masses respectively is entirely different at different times of the year. This is partly due to the differences in temperature (and other physical factors) between the penetrating air mass and the existing air mass above the penetrated region at different seasons. It is due partly to the physiological changes in the thermoregulating system at different periods of the year (see p. 472).

(4) It was pointed out on p. 334 that in a normal person *diuresis* increases sharply after the influx of cold air masses and decreases with warm air masses. During a preliminary study of the daily diuresis of schizophrenics at the Psychiatric Institute Endegeest (near Leiden), covering the period from 18th Dec. 1959 to 1st May 1960 (using 4 male schizophrenics), an abnormally functioning thermoregulation system was observed, *i.e.* a *considerable increase in diuresis during periods of temperature rise* and *vice versa*. This change in water retention may be partly responsible for the unrest of schizophrenics during the influx of warm air masses, as suggested by the low-pressure experiments of Smith (see p. 297), indicating that a drop in atmospheric pressure causes water retention accompanied by restlessness in bitches.

(5) The water-bath test devised by Henschel *et al.* was described on p. 254 indicating that schizophrenics exhibit a prolonged latent period before vasodilation begins as compared with normal persons. Henschel assumed that schizophrenics either have an exceptionally high and persistent state of tonus in the skin vessels or an abnormally high temperature threshold in the hypothalamus. In both cases the thermoregulation mechanism in schizophrenics works differently from that of normal persons.

The daily fluctuations may be partly due to clinical factors, in particular errors in registration due to changes in temper of the observing staff. However, as the clinical material of the same day of several clinics or of several independent departments of the same clinic are united, this local factor could be eliminated.

Oligophrenia (debilitas mentis, imbecillitas and idiocy)

(1) The daily and monthly percentages of restlessness are of the same order of magnitude as in the case of schizophrenics.

(2) The *pseudo-seasonal fluctuations*, although less pronounced than in schizophrenics if the averages for each month are compared, show the same early winter peak if the average for three-month periods are taken into consideration. For example:

Nov.	1956 – Jan.	1957:	average	monthly	restlessness	16.0%
Feb.	'57 – April	'57:	average	monthly	restlessness	11.8%
May	'57 – July	'57:	average	monthly	restlessness	7.0%
Aug.	'57 – Oct.	'57:	average	monthly	restlessness	9.1%
Nov.	'57 – Jan.	'58:	average	monthly	restlessness	9.7%
Feb.	'58 – April	'58:	average	monthly	restlessness	8.1%
May	'58 – July	'58:	average	monthly	restlessness	2.4%

During the same period the average percentages of restless schizophrenic patients were: 14.5, 10.0, 7.0, 7.1, 11.4, 6.3 and 4.4%.

(3) The *daily fluctuations* of the restlessness curves sometimes coincide with those of the schizophrenics, particularly during the winter season, but often also differ considerably. Whereas schizophrenics are hardly affected in their restlessness by unpleasant weather conditions, the oligrophrenics are considerably affected and this purely psychological effect may also give rise to considerable restlessness during periods of cold air influx.

Epilepsy

Two different weather relationships were studied by the author, *viz.*, the influence of weather and climate on the restlessness of epileptics and on epileptic seizures.

(1) *Influence on restlessness.* (*i*) The pseudo-seasonal fluctuations suggest a maximum around November–December and a minimum in summer; sometimes there is a secondary maximum in May. For the three-month periods of Nov. '56 – Jan. '57, etc., as indicated above, the average percentages of restless patients were 11.5, 5.7, 7.3, 4.0, 15.6 (Nov. '57–Jan. '58), 5.1, 3.2 and 5.7. (*ii*) The relationship between daily restlessness and weather was not convincing.

(2) *Influence on seizures.* (*i*) The seasonal fluctuations in seizures were very pronounced in the case of some patients among a group of 79 in certain years between 1949 and 1956, but no relationship whatever was found applicable to other patients or other periods. The lack of consistent seasonal phenomena is not surprising, since the large number of patients observed belonged to a group living for many years in a psychiatric institute and treated continuously with drugs. (*ii*) An analysis, with the Integral of Probability of Gauss (see p. 175), of the possible relationship between *weather fronts and epileptic seizures* in a group of 79 patients at Leiden, in 1956, has shown a statistically significant increase in the number and degree of epileptic attacks after the passage of cold fronts. No significant deviation from chance expectation was observed after warm fronts. The association with cold fronts becomes particularly significant if one takes only days of epileptic attacks 50% or more above the monthly average in account. (*iii*) The influence of *differences in light intensity* was not studied, but it may play an important part in these phenomena. It is known that an epileptic walking along a road with closely spaced high trees on a sunny day may have a seizure brought on by the rapid flashes of light. The American Air Force observed the same as the result of aeroplane propellers causing high frequency flashes of light. Recent studies have shown that certain frequen-

cies have a stimulating effect, whereas frequencies of 10-16/sec have a detrimental influence (p. 451). In this connection we may refer to p. 207, where the physiological mechanism of meteoro-hypnotic conditions was described.

3. Possible Causes of Meteorotropic Restlessness of Mental Patients

Changes in the physico-chemical state of the blood of schizophrenics

Studies by Chapman and Wolff[2551a] suggest significant alterations in metabolism of the brain of schizophrenics, which would be reflected in the physico-chemical state of the cerebrospinal fluid and blood serum. Whether these changes are only a manifestation of deranged metabolic function of the brain or a causative factor in such a derangement is difficult to say at present. However, in both cases these changes may affect the functioning of the brain and the behaviour of schizophrenics.

Studies by Tromp of the physico-chemical state of the blood of schizophrenics have shown the following characteristic differences from normal persons: (*i*) The total amount of proteins, the α-globulin, calcium and phosphate level of the blood serum, is the same as in normal persons. (*ii*) The albumin level is low (although not pathological), particularly in patients above the age of 50 (*e.g.* values of 60% against 69% in normal persons). Whereas in normal persons the albumin level is very constant for considerable periods, fluctuations of 10% within a month were common in schizophrenics (*e.g.* a 67% albumin level may change into 57%). These relationships apply to all psychiatric institutes which have been studied and are not affected by the number of years that the patient has been living in the institute. In other words, differences in diet (which were well balanced in these institutes) cannot account for this albumin deficiency. (*iii*) The β- and γ-globulin levels were usually higher than normal. (*iv*) The blood sedimentation rate in many completely healthy (except mentally) schizophrenics is often very high (20 or more mm during the first hour, see p. 317. (*v*) So far, these changes have not been observed in the physico-chemical states of the blood of oligophrenics and epileptics.

The peculiar physico-chemical properties of the serum and urine of schizophrenics were also demonstrated by Fischer[2657a] in Canada, in 1953. Fischer observed that if 10–20 ml/l of serum or 25–50 ml/l of urine of schizophrenics was added to the water medium of 14-days-old larvae of *Xenopus levis Daudin* (a tadpole also used for pregnancy tests), bred at 20° C, a significantly higher mortality occurred than if serum or urine of normal persons were added in the same dilutions. This toxicity of the serum of schizophrenics disappears after exposure to 50° C for 30 minutes; urine maintains its toxicity even after being boiled for 30 minutes. Fischer noticed that the difference in toxicity between the serum of schizophrenics and normal persons becomes insignificant on days of drastic weather changes as a result of passages of weather fronts.

The influence of weather and climate on the physico-chemical state of the blood was discussed on pp. 275, 316 and 318. In view of the peculiar physico-chemical properties of the blood of schizophrenics, the possibility that these meteorotropic changes are, at least partly, responsible for the change in behaviour of schizophrenics during the influx of warm air masses cannot be ruled out.

Dysfunction of the thermoregulation system in schizophrenics

It has been pointed out that, after heat stress, vasodilation requires a prolonged latent period in schizophrenics. Diuresis is not reduced as would be expected, but may increase considerably. In view of the close functional connection between the hypothalamic-hypophysial system and the rhinencephalon (see p. 302), it would not be surprising if emotional disturbances were created, causing increased restlessness. Nevertheless, a considerable amount of research is still required for a more detailed explanation of these observations.

Influence of sunlight on restlessness of schizophrenics

The fact that schizophrenics as well as oligophrenics and epileptics display their maximum unrest in the cold period of November to January, although this is not the coldest time of the year, suggests that, in addition to temperature, the considerable diminution of sunlight in late autumn to early winter may be responsible for this pseudo-seasonal phenomenon.

In October the number of sun hours in the Netherlands is 105, in November only 53, in December 44, in January 54, in February 76. The purely psychological influence of this lack of sunlight may undoubtedly affect the general mood of many normal healthy persons in this period of the year. However, as pointed out on p. 537, the restlessness of schizophrenics does not seem to be affected by unpleasant weather conditions, so there is little reason to assume that the shortage of light would have a different psychological effect. On the other hand, there are the various physiological effects of a decrease in sunlight as summarised on p. 347. It seems more likely that, at least in the case of schizophrenics, this light factor is an important element in the causation of the pseudo-seasonal fluctuations in restlessness.

Possible causes in epileptics

In epileptics, other mechanisms are probably involved. Immediately preceding the clinical onset of symptoms, known as *petit mal* and *grand mal*, a drastic change in brain potentials (see p. 206) takes place. Electroencephalographic studies suggest that in epilepsy there is a disturbance of the mechanism, normally regulating the resting rhythm of the cortical nerve cells. Such a "paroxysmal cerebral dysrhythmia" may be induced by hyperpnoea and hypoglycaemia and apparently also by light flashes of a certain frequency, causing an overstimulation of the optical nerves. The influence of cold fronts, on the other hand, suggests that a dysfunction of the hypothalamus is mainly responsible for the meteorotropic effects.

4. *Influence of Weather and Climate on Apoplexy, Mental Deficiency and Low I.Q. of Children, Insomnia, Migraine and Suicide*

Apart from the meteorotropic phenomena observed in schizophrenics, oligophrenics and epileptics, a number of other interesting mental diseases have been studied in relation to weather and climate.

Apoplexy

The seasonal fluctuation of mortality from apoplexy in males and females and the possible influence of thermal stress on this disease was discussed on p. 507. For further details see the refs.[2571–2581].

Mental deficiency and low I.Q. of children

This very important social problem was already briefly reviewed on pp. 535 and 674. See also the refs.[2680–2681].

Insomnia (abnormal wakefulness)

The influence of weather on sleep, although very likely, has not been established experimentally beyond doubt. This is partly due to the fact that the whole physiological mechanism of sleep is only partly understood.

Physiological phenomena accompanying sleep

During sleep there is a fall in blood pressure; decrease in heart rate; the respiratory rate is very regular and usually reduced, but may remain unchanged or even increase; the CO_2 tension in the alveolar air and arterial blood is raised due to decreased lung ventilation; the metabolic rate is lowered; usually a smaller volume of urine is secreted associated with acidaemia; skeletal muscles are usually markedly relaxed (except of the bladder, eyes, etc.); the pupils are small; the recording of external stimuli is considerably reduced; the α-waves in the electro-encephalogram become slower, larger and less irregular and may even disappear in deep sleep (see p. 207).

The evidence of recent electro-encephalographic studies in the Mount Sinai Hospital (New York) suggests that, during the night, a normal person has 4-5 periods of dreaming, comprising about 20% of the total sleeping period. Disturbances occurring during these periods of dreaming create serious psychological disturbances the following day, whereas no detrimental effects were observed if the person woke up between periods of dreaming.

During sleep the autonomic nervous system continues to function, although there is a considerable shift to the parasympathetic nervous system. It is mainly the somatic nervous system, in other words the higher parts of the brain and cortex, which are reduced to comparative quiescence.

It was pointed out on p. 312 that the essential manifestations of unconsciousness are regulated, at least partly, by certain areas of the rhinencephalon. According to one of the theories of sleep, the quiescence of the cortex is due to blocking of the thalamus (see p. 207). Because of its location, the functioning of the thalamus is closely associated with the hypothalamic activities. Stimulation of the mamillary nuclei (see pp. 202 and 203) produces sleep. On the other hand, environmental stimuli during the night, causing a dysfunction of the hypothalamic nuclei, may disturb sleep, for which reason this part of the brain is often described as the *sleep centre*.

Hess (*Helv. physiol. pharmacol. Acta*, Suppl. 4, 1947), using cats for his demonstration, showed that stimulation with micro-electrodes of the grey matter extending backwards from the thalamus, induces sleep. If the stimulation is discontinued, the animal wakes up. Conversely stimulation of closely adjacent regions (only 1.5 mm apart) may give rise to bursts of activity. Recent studies by Parmeggiani have confirmed the findings of Hess. As dogs and cats are able to sleep even after the removal of the cerebrum (see p. 188), the areas comprising the "sleep centre" are evidently more necessary to the inducement of sleep than is the cerebral cortex.

Although most physiologists agree that the function of sleep is to enable the body to recuperate from the effects of the daily activities and environmental stimuli, the deeper physiological mechanisms involved are not yet known.

As many people are accustomed to sleeping with the window open and since drastic changes in weather can affect the indoor microclimate (see p. 82) even when the windows are shut, *sleep could be disturbed by at least two meteorological factors*, apart from the mechanical noises attendant upon a storm:

(1) *Influence of changes in the thermal equilibrium of the bedroom.* A sudden influx of *cold air* during the night, particularly if accompanied by increased air turbulence, will lower the temperature around the bed. As a result, more heat is drained from the human body and its enveloping blankets. Owing to the lowered metabolism and less effective impact of external stimuli during sleep, continuous cooling around the bed may cause a disturbance of the thermoregulation centres in the hypothalamus, which in turn may affect the thalamus and other parts of the sleep centre. The influx of *warm air* masses, particularly with decreased air turbulence, may cause excessive accumulation of heat under the blankets and this too may disturb hypothalamic functioning.

(2) *Influence of fog.* A fog which begins during the night may have two effects disturbing sleep: (*i*) Bronchitics, or people suffering from other pulmonary disabilities, may become oppressed. The disturbance of the breathing centre may wake up the sleeping person. (*ii*) Air polution and fog may be distinctly odoriferous and stimulate the rhinencephalic areas during sleep.

There appears to be little doubt, therefore, that insomnia may also be a meteorotropic phenomenon, although few systematic studies have been carried out in this field (see refs.[2652, 2653]). Studies by Ungeheuer, Amelung, Becker and others suggest that insomnia is a common phenomenon during periods of occlusion (see p. 19).

Migraine (hemicrania)

This one-sided headache, usually accompanied by nausea, vomiting, dizziness, yawning and increased sensitivity of the eyes, etc., may have various pathological causes, but is often purely psychological and is particularly common after a previous concussion of the brain, especially if the patient has not taken sufficient rest. These two latter forms of migraine are most common during drastic changes in weather, just before heavy snowfall, thunderstorms and so forth. Very little is known, however, about the physiological mechanisms involved.

Suicide and crime

Various reports in the U.S.A. suggest an increase in suicides during May. In the Northern parts crimes against property seem to be high in winter, whereas crimes against persons reach a maximum in summer. As many complex sociological factors are involved in these phenomena and many suicide trials are never reported to the police if no serious consequences occurred, it is extremely difficult to study these problems on a scientific basis.

De Rudder[6, p. 59] and Tholuck[2679] studied 200 cases of suicide, recorded during 1939 at the Institute of Forensic Medicine of the University of Frankfurt (Germany). Whereas no relationships could be established with atmospheric pressure, temperature, hours of sunshine and precipitation, a highly significant correlation was found with weather fronts, both cold and warm. On days when fronts were passing over the country, the n-method gave a value for $d = 6.3\ \sigma_d$ (see p. 178).

Studies by Rohden[2678] and others, in Switzerland indicate a significant increase in cases of suicide and crimes in periods when the foehn prevails (see p. 24).

Reiter[2677] was able to demonstrate a statistically significant correlation between days or periods of high frequency of suicide and days of strong disturbance of long electromagnetic waves (see p. 79).

Although little is known about the physiological mechanisms involved, it seems most likely that considerable disturbances of the hypothalamic-pituitary system as a result of drastic changes in weather are involved in these meteorotropic cases of suicide and crime.

Subsect. H. RHEUMATIC DISEASES[2685–2951]

1. Classification

As rheumatic diseases are not a sharply defined group, all physicians do not adhere to the same classification and definition. Rheumatism is often defined as a disease affecting the connective tissues, marked by pain or stiffness in joints, muscles and related structures, usually recurrent and often due to exposure, which may be acute or chronic. The disease seems to be more common among females than males. The incidence of this group of diseases varies considerably in different parts of the world, but also in the same country. Occupational differences have also been observed, *e.g.*, a high incidence has been reported among brewers and metal workers, whereas the incidence is low among sailors and fishermen. Studies in Sweden and the Netherlands, where the population does not migrate to any large extent, suggest that 20–30% of the morbidity in these countries is due to one or more varieties of rheumatic diseases, particularly in the age group of 50 and older*. In 1916, 1% of the population in Sweden was permanently

* In 1956 about 11 million people in the U.S.A. were suffering from one form or another of rheumatic diseases of whom 300,000 were temporarily unemployable.

In Great Britain £ 40,000,000 were lost in 1949 due to serious illness as a result of rheumatic diseases.

invalided as a result of rheumatic diseases. Notwithstanding this very high incidence and the general belief of both rheumatics and physicians that weather and season affect the severity of the complaints, relatively little is yet known of the exact influence of meteorological conditions on the origin and development of rheumatic diseases.

The various rheumatic diseases have been classified (into two groups) as follows by a number of experts serving in the World Health Organization:

Truly rheumatic diseases

(1) *Localised in the joints*: (*i*) Due to inflammation: acute rheumatism (rheumatic fever), rheumatoid arthritis (polyarthritis), ankylopoetic spondylosis (Morbus Bechterew), etc. (*ii*) Due to degeneration: arthrosis deformans (osteoarthritis).

(2) *Not localised in the joints* (due to inflammation): fibrositis, bursitis, myositis, tendosynovitis, periarthritis.

Para-rheumatic diseases

Various collagen (collagen is the main supportive protein of connective tissue) and other diseases with rheumatic characteristics such as lumbago, podagra (gout), myogelosis, etc.

For the non-medically trained bioclimatologist the following definitions may be useful:

Arthritis: an inflammation of the joints due to bacterial infections or injuries (either caused by a simple severe mechanical injury or an endless repetition of minor unnoticed injuries, mechanical or physical).

Acute rheumatism (or *rheumatic fever*): an acute arthritis, common in children, particularly in the larger joints, often accompanied by rheumatic inflammation of the lining or muscles of the heart and by high fever.

Rheumatoid arthritis (or *polyarthritis*): a polyarticular arthritis, chronic or recurrent, often symmetrical on hands and feet, common in women between 20 and 40.

Ankylopoetic spondylosis (or *Morbus Bechterew*): an inflammation leading to immobility and consolidation of the vertebral column and hip-joints.

Arthrosis deformans (or *osteoarthritis*): a degenerative joint disease, particularly in knee and hip-joints, of unknown cause, particularly common at the age of 60 and older and leading to immobility.

Fibrositis: an inflammatory hyperplasia of the white fibrous tissue of the muscle sheaths.

Bursitis: an inflammation of the sac that helps to reduce the friction around a joint.

Myositis: an inflammation of muscle tissues.

Tendosynovitis: an inflammation of a tendon (the fibrous cord by which a muscle is attached) and its sheath.

Periarthritis: an inflammation of the soft tissues surrounding a joint, accompanying arthrosis deformans.

Lumbago: acute rheumatic pains in the lumbar region, usually due to one-sided muscular rheumatism.

Podagra (*gout*): painful disease of the joints due to the body's inability to dispose of its purines (the basic compound of uric acid). The excretion of uric acid increases during an attack.

Myogelosis: a hardening of the muscle substance.

2. *Influence of Meteorological Factors*

It will be clear from the previous summary of the varieties of rheumatic diseases that it is probably not one particular meteorological factor that influences rheumatic diseases in general. Every biometeorological study should sharply distinguish between the various diagnoses and sexes. As diagnoses in different countries and even in different parts of the same country may differ considerably, so far it has been very difficult to compare the published reports. Nevertheless, a number of important observations have been made which, despite the heterogeneous character of the data, may give us a clue to the effect of weather and climate on various rheumatic diseases and to the physiological mechanisms involved.

General statistical studies

As far back as 1816 Balfour[2693] called attention to the association of rheumatism with changes in the weather. In the refs.[2685-2951] a number of publications are cited in which the statistical relationship between weather and rheumatic complaints are discussed.

Everett[2745] published an interesting study in 1879. He observed many cases of traumatic neuralgia, chronic neuritis and chronic rheumatism over a period of $12^1/_2$ years. His results indicated a correlation between increased pain, storms (either with or without rain and snow) and falling barometric pressure. Humidity alone did not seem to affect the degree of pain. The intensity of the pain was in proportion to the nearness of the storm and the abruptness of its onset. A similar study was published by Mitchell[2816] in 1877 based on a record of $3^1/_2$ years of daily observations made by an army officer who suffered from neuralgia following amputation of a leg. Pains increased even before the onset of the storm.

On the 365 days of 1927, Rentschler *et al.*[2841] studied the daily records of the clinical status of 367 patients suffering from arthritis in the Mayo clinic, in relation to fluctuations in barometric pressure. Three-hundred of these patients suffered from non-specific infectious arthritis, 32 from gout and 35 from senescent and other types of arthritis. Only subjective observations concerning changes in pain or stiffness were used. The observations were recorded before the barometric observations were made, in order to avoid mental bias. The following results were obtained: (*i*) Pain associated with senescent, traumatic and gouting arthritis was seldom related to changes in weather. (*ii*) Seventy-two percent of the time, the group of patients as a whole suffered more pain with falling barometric pressure and were relieved with rising B.P; 21% of the time the reverse was observed. (*iii*) The pain curve of one of the patients alone ran parallel with the barometric curve for 77% of the time and for 20% in an inverse direction. This relationship kept up for $2^1/_2$ months, then ceased temporarily following a minor operation. In other cases these relationships were even 81% (parallel) against 15% (inverse). (*iv*) During periods when the pain curve was not in accord with the barometric curve, it was usually related to storms or marked changes in weather (apart from B.P.). (*v*) During 90% of the year storms were associated with increased pain; pains decreased on clear sunny days. The stormy effect was often observed before the storm began or changes in cloudiness or sunshine could be observed. (*vi*) Humidity changes alone do not seem to be correlated with the pain curve.

More recent biometeorological studies, described in the previous pages, suggest that probably it is not the barometric pressure itself which is responsible for the observed relationship. In this region of the U.S.A. a change in barometric pressure is probably a biometeorological indication of abrupt changes in air mass, cooling, etc.

In 1926 Feigl and Freund[2750] studied 2042 cases of acute rheumatic attacks in Breslau (Germany). No corrrelation could be established between rheumatic attacks and single meteorological factors, but a significant increase in rheumatic complaints occurred during the passage to both warm and cold fronts, although the influx of cold polar air had the greatest effect.

Extensive studies by Köhler and Flach[2792] in 1932, confirmed by Franke[2757, 2758], revealed a number of interesting statistical relationships: (*i*) During the first acute attack (*e.g.* acute polyarthritis) no meteorotropic sensibility was observed. (*ii*) At later stages the degree of weather sensibility, preceding the actual change in weather, differs for each patient both in time and number of observed weather relationships. For example, the influx of warm air masses is observed 2–4 hours before the influx; that of a cold air mass 5–10 hours before. Depending on the microclimate surrounding the patient during the period of influx, the changes in weather can be predicted regularly or only in a number of cases. (*iii*) The more rapid and violent the changes in weather, the smaller are the individual differences in weather sensibility in a group of rheumatic patients. As cold fronts are often more active than warm fronts in Germany, individual differences will be smaller during the passage of cold fronts. Ungeheuer and Stollreither[2864] also observed a relationship between the severity of complaints and the rate of change in weather phases (see p. 24). (*iv*) Franke[2758] studied microscopically the capillary changes in the skin of rheumatics during changes in weather and found objective changes in the capillary structure. Similar observations were made previously by Bettmann[1382, 1383] in 1930. He observed uncoordinated vasomotor changes *(dysergia)* in the skin of people sensitive to changes in weather. Under the microscope he observed the appearance or disappearance of capillaries, *e.g.*, before an approaching thunderstorm. These changes disappear and the capillary pattern becomes normal again after the storm is over.

The daily variation in rheumatic complaints of a group of 35 out-patients was studied by Tromp at Leiden, from November 1956 to July 1958. The diagnoses were established by the Department of Rheumatology of the University Medical Centre, Leiden. These patients comprised about 15 suffering from rheumatoid arthritis, about 10 from arthrosis deformans, 4 from Morbus Bechterew, the remaining 6 suffering from lumbago, myogelosis, etc. In each group there was about an equal number of males and females. Each patient daily (for the four periods 0–6, 6–12, 12–18, 18–24 h.) filled in a special form stating his subjective complaints and other important data, such as medical treatment, general health (cold, influenza etc.), psychosomatic factors (difficulties at home, in the office), holidays and so on. The daily percentage and severity of complaints for each diagnosis and sex were calculated from these lists. In view of the relatively small number of cases, the results cannot be called conclusive, but the assumption of a biometeorological relationship received considerable support from the observation of this group of patients for almost 550 consecutive days. The most important preliminary conclusions are the following: (*i*) There seems to be a pronounced difference in the daily number of complaints for the different diagnoses, but the complaint curves for the males and females of the same group of diagnoses also often differ considerably. (*ii*) Whereas substantial daily variations were observed in the arthritis group, the percentage and severity of complaints of arthrosis patients suffering from arthrosis remained fairly of complaints of patients suffering from arthrosis remained fairly constant for considerable periods. (*iii*) The best weather relationships were the percentage of complaining patients, at times of falling temperature, strong winds, the passage of cold fronts and influx of polar air masses. (*iv*) This relationship was less clear in females and the increase in complaints was often retarded as compared with the male group. (*v*) Sometimes, too, the complaints of patients suffering from arthrosis, like those in male arthritic patients, were exacerbated during falling temperature, etc. (*vi*) Observations did not disclose a distinct seasonal association, although a gradual decrease in the monthly average of complaints of male arthritics was observed in 1957, for example, from January (65%) to May (21%), followed by an increase. During this whole first part of 1957 the average monthly temperatures were about twice the normal values, whereas in from May the first periods of temperatures below normal began.

Influence of humidity

It was pointed out on pp. 35 and 223 that humidity as such has little effect on our skin temperature. Humidity changes in the environment may, however, affect human comfort indirectly owing to changes in thermal conductivity of the skin near the thermal receptors, differences in evaporation of clothes, change in the infra-red radiation of the walls and floors of rooms in buildings (see p. 37).

Several authors, *e.g.* Van Breemen in the Netherlands, Miller and Fox in England, Teissier and Roque in France and Natvig in Norway, noted a very high incidence of rheumatic diseases among thousands of patients living in damp houses. People living in damp basements are particularly prone to chronic rheumatism. Soldiers who spent a considerable time in wet trenches during the war often returned as chronic rheumatics. On the other hand, physical labour in a very humid environment seldom has harmful effects, which may account for the low incidence of rheumatic diseases among those whose work has to be done in a humid environment.

In October 1951 De Blécourt[2949] recorded the incidence of rheumatic diseases in relation to humidity in 175 houses in the Northern part of the Netherlands. The degree of humidity was determined by measuring the electric resistance of the walls. Rheumatism occurred in 46% of the damp houses, but also in 57% of the dry houses. However, as the electric measurements often do not give an accurate picture of the dampness of a wall and, seeing that the important point is the *local* humidity of a bedroom or office where people spend most of their time, rather than the general humidity of a building, these results can hardly be said to refute the vast number of data mentioned above.

During a more recent study for the National Research Council, between 1957 and 1960, Varekamp[2950] of Leiden (the Netherlands) found a statistically highly significant correlation between the incidence of rheumatoid arthritis and houses where there was considerable wood-rot* in the floors due to wood-decaying fungi. Seven cases occurred in one street, all living in houses built on poorly drained soil and low floors which were at groundwater level in winter. Although Varekamp found no direct evidence that the wooden

* Wood-rot is actually due to a growing mycelium of wood-decyaing fungi (particularly *Basidiomycetes*) which requires a certain, rather constant, degree of moisture of the wood, with little evaporation. Temporary high moisture content followed by evaporation and dryness does not necessarily cause wood-rot (see also Varekamp[2950]). The wood-rot fungi require a special humidity of the wood (fluctuating between 20 and 70%), certain temperatures (min. 4° C, max. 27 35° C, optimum 22-27° C), sufficiently humid air around the wood, little air movement and darkness. Wood-rot in the ground floors is very common in Holland, but rare in other countries in N.W. Europe, where the same fungi are often found in the upper floor of the building.

floors in the houses riddled with wood-rot were damper than others (the humidities of the walls were not measured) very great humidity of the soil and floor is almost bound to prevail in all houses where there is advanced wood-rot, at certain periods at all events.

Observations by the author, using infra-red (heat) wave detectors, indicate that, although a wooden floor in a room may be dry everywhere and there may even be an air space of 2 or 3 feet between the floor and a damp concrete basement, the most humid parts of the basement can be detected above the dry wooden floor because of a local decrease in infra-red radiation. A rheumatic is sensitive to such spots. It was pointed out on p. 474 that a similar study of wood-rot by Varekamp and Voorhorst at Leiden demonstrated a statistically significant relationship between houses in which it prevails and patients suffering from atopic asthma (see p. 465).

The indirect influence of the humid micro-climate on rheumatic diseases is also suggested by various medico-geographical studies indicating that less rheumatism seems to occur in areas located on dry sandy soils with good groundwater drainage.

Influence of soil

At the Eastbourne Public Health Congress held in England in 1933 an extensive discussion took place on the relationship between soil and climate and rheumatic diseases. It was reported that the greatest incidence of juvenile rheumatism occurred in England on soils along the course of rivers or near former watercourses. In the State of New York the smallest number occurred in districts furthest away from the river. A study by the medical research council in St. Thomas's Hospital, London, indicated that a large portion of the patients suffering from rheumatic fever lived within half a mile of the Thames or other waterways. In England clay soils apparently tend to promote juvenile rheumatism, although there is not sufficient statistical evidence to support this assumption.

The following observations point to a possible relationship between soil, micro-climate and rheumatism. Electric soil surveys by the author in the Netherlands between 1946 and 1960 indicate that usually every area is crossed by one or more zones of high electric soil conductivity, or low soil resistivity. These zones are caused by various geological conditions, *e.g.* the presence of underground fractures or faults; old river valleys in a sandy soil filled up with clay; an abrupt local rise of a peat layer under a horizontal stratum of clay, etc. In all these cases, owing to a locally higher moisture content (and often also higher content of humic acid), the soil resistance drops considerably, *e.g.*, from 70,000–5,000 ohms/m.

Patches of damp will occur in the basement of a house built above a moisture zone of this kind and these may show up as increased humidity of the floor here and there on the first storey, or as locally diminished infra-red radiation. Physiologically pre-disposed subjects spending many hours in parts of a house where such conditions prevail may be liable to become rheumatic (see p. 37).

Influence of temperature

The various observations described on pp. 547 and 549 clearly indicate that rheumatic diseases are rare in an environment of relatively high temperature, provided there be no considerable cooling due to great humidity and air turbulence. This is why people in some tropical regions, who fail to take the necessary precautions after perspiring profusely and then cooling down, present symptoms of rheumatism.

3. Physiological Mechanisms Involved

The summary given on p. 546 indicates a variety of causes for the development of rheumatic diseases. However, inflammation of the joints, or of the tissues and muscles surrounding the joints, is the principal characteristic of arthritic diseases. It was pointed out that these inflammations are tissue responses to injury either by bacteria or viruses, or by chemical, physical or mechanical trauma. The inflammation is evidenced by vascular dilatation, fluid exudation or accumulation of leucocytes (see p. 515), or any combination of the three. Meteorological factors could affect these various causes of injury in two different ways, *viz.*:

Lower general resistance to infectious diseases with consequent proliferation and spread of micro-organisms and viruses

The various mechanisms involved were discussed on pp. 513–522. Changes in temperature (combined with humidity and air turbulence) and ultraviolet solar radiation have proved to be the chief meteorological agents affecting these factors.

Drastic thermal changes in the physical environment

Various physiological mechanisms are probably involved in the causation of thermal injury leading to rheumatic pains.

(1) *Disturbance of the thermo-regulation mechanism.* It is known that rheumatics are usually very sensitive to cooling effects and warm up slowly after being cooled, both phenomena being due to inefficient and retarded contraction or dilatation of the peripheral arteries. If rheumatic and normal persons come into a cold room, the skin temperature of the former drops

more slowly than that in the latter; but it takes longer for the body temperature to rise in a warm room. The first extensive study on the thermo-regulation of rheumatics was carried out by Tichy[2867a] at the Institute of Rheumatology in Dresden (Germany), in co-operation with Mierisch and Warmbt. Forty-five people (10 normal persons and 35 rheumatics) were heated in a sauna bath for 10–15 minutes in 190 experimental periods. In 69% there was a normal gradual rise in skin temperature; in 13% a fairly constant temperature set in after an initial rapid rise. These people can endure considerable environmental heating without discomfort. In 18% there was a steep rise in temperature quickly reaching (usually in 10 minutes) the limits of comfort. This latter, thermally intolerant type seems to be more common among males than females and predominated among patients suffering from chronic rheumatism. Although the material is still too small to allow of definite conclusions and the tests described on pp. 251–255 would appear to be more efficient for accurate thermo-regulation tests, the results obtained so far support the view that rheumatics often have a poor thermo-regulation system. The reported lower incidence of juvenile rheumatism in country, as compared with urban children, may be due to their better acclimatisation to cooling from early childhood.

The assumption of such fundamentally different functioning of the hypothalamus and other important centres of the brain (*e.g.* rhinencephalon, see p. 309) in rheumatics is supported by the psychosomatic studies made by Prick and van der Loo at Nijmegen (the Netherlands), in 1959. They observed in patients suffering from chronic rheumatoid arthritis an increased susceptibility to emotional stimuli from the environment. Hypothalamic and endocrinal dysfunction were often found, though the authors could not discover whether these changes are primary or secondary effects.

In this connection the observations of Stewart *et al.*[2870a] in Oxford are also of great interest. They studied 598 cases of rheumatic carditis, 1308 of rheumatic fever without evidence of heart involvement and 1303 with less precise diagnoses, such as arthritis, fibrositis, etc. It was found that the incidence of rheumatic carditis is three times greater in light than in heavy persons and nearly four times greater among slender men (Sheldon's ectomorph type). Some indications were found that slender men are also more prone to arthritis. The relationships between body-build and thermoregulation were discussed on p. 230. According to Fletcher[2752] infective arthritis also seems to be more common in the asthenic, pale individual, whereas arthrosis deformans is common in the stout, possibly lethargic person.

A dysfunction of the thermo-regulation mechanism is usually accompanied by a difference in functioning of the adrenal gland, which shows up if, for example, a daily 17-KS analysis of the urine is made (see p. 328). The influence of these various adrenal hormones on certain muscle enzymes is discussed on p. 555.

(2) *Disturbance of mucoprotein metabolism.* In 1957 Kamiyama *et al.*[2789] studied the influence of weather in Japan on the metabolism of hexosamine (a derivative of muco-proteins, see p. 247), which is found in the joints, other cartilages and the blood of rheumatics. A relationship was reported by others with the amount excreted in the urine and the clinical conditions of rheumatic patients. During painful periods the amount would be high and, therefore, more would be secreted in the urine, whereas the amounts decreased after treatment with adrenocortical hormones. At the same time the difference in vasomotor reflex was studied with a plethysmograph in 3 healthy and 3 rheumatic males after a bath of 40° C. The following was observed: (*i*) The amplitude of the pulse waves in the plethysmogram of the healthy person was noticeably larger than that of the rheumatic patient after bathing. (*ii*) Both in the healthy and rheumatic patient the amplitude increased during bathing; the enlargement ratio was greatest in rheumatics. (*iii*) If a person, whose neck was moistened with a wet towel, was subjected to an artificial air current and both the finger temperature and plethysmogram were recorded, a higher correlation coefficient was observed in healthy people than in rheumatics. (*iv*) The daily amount of hexosamine secreted in five rheumatics during 30 days suggest that just before the passage of a low pressure area the secreted values were low followed by a steep rise after the passage. As also the secretion of 17-KS (and probably other adrenal hormones) changes with the influx of different air masses (see p. 328), there may be a relationship between weather–adrenal hormones–hexosamine and rheumatic complaints, which will be different depending on the degree of dysfunction of the thermoregulation system.

(3) *Disturbance of enzyme activity.* It is known that during muscular contraction and relaxation a series of chemical processes occurs which is responsible for part of the heat production in the body (see p. 212). During these exothermic (heat producing) reactions, one of the important constituents of the skeletal muscles, *adenosine triphosphate (ATP),* is broken down by an enzyme, *adenosine triphosphatase,* into adenosine diphosphate and phosphate. Recent studies by Racker *et al.*[2836a] in the U.S.A. have shown that temperature stress has an important effect on these enzymes. (*i*) It was found that the activity of ATP-ase rapidly decreases at +4° C. ATP protects the enzyme against inactivity by great heat and dialysis, but it apparently does not protect the enzyme against cold. (*ii*) The activity of the enzyme depends also on the magnesium level of the blood.

(4) *Changes in viscosity of the synovial fluid and cellular permeability.* On p. 247 the studies of Hunter[2777, 2778] were described, indicating that cooling causes the greatest fall in temperature in joints, followed by muscles and skin. After heating, the joints exhibited a prolonged recovery period. As this recovery process depends on the efficiency of the thermo-regulation mechanism, it will obviously take the longest time in persons with a poor thermo-regulation system. It was also found that cooling decreases cellular permeability and that therefore the removal of metabolic waste products is retarded.

The membrane permeability is associated with *hyaluronidase* (according to Duran-Reynals, *Bact. Rev.* 6, 197, 1942), an enzyme which facilitates the breakdown of *hyaluronic acid*, the cause of increased tissue permeability. Hyaluronic acid comprises a group of muco substances, discovered by Meyer and Palmer in 1934, which consist of uronic acid and N-acetyl-glucosamine, the concentration in tissue fluids being 0.009–0.048%. It is probably produced locally by mast cells (see p. 286) and young fibroblasts.

The activity of hyaluronidase enzyme is inhibited (breakdown of hyaluronic acid reduced) by various hormones of the adrenal cortex; *e.g.* cortisone (see p. 278). But cortisone does not only *reduce membrane permeability*; it also *reduces the amount of chondroitin sulphate*, a sulphate ester of aminopolysaccharides, which occurs in the lubricating joint fluids secreted in anatomical cavities and known as *mucin* (see p. 247). The chief viscosity-raising agents in mucin are mucoproteins (the derivatives being known as hexosamines,) and mucopolysaccharides. The muco substances are formed by association of the major proteins, polysaccharides and lipoids. During rheumatoid conditions a derangement of these various components of mucin are observed and a surplus of hexosamines is secreted in the urine.

Falling temperature increases the viscosity of the synovia, particularly if the fluid has a high mucin content (depending on the pH of the fluid), increasing the frictional resistance against joint movement. Experiments performed by Hunter *et al.*[2778] on healthy males confirmed that, for a given fall in skin temperature over the proximal interphalangeal joint, there was an equivalent reduction in the number of finger movements required in their "push-button experiment".

(5) *Stimulation of the autonomic nervous system.* If normal *deep tissues* are cooled rapidly from 30–15° C, deep pain is experienced (Coleman,). As cooling proceeds, analgesia (absence of sensibility to pain) develops, which becomes complete at a tissue temperature of 10° C. The same cooling taking place slowly, hardly causes any pain in a normal person whereas even slow cooling may cause in rheumatics pain, because in them the adjustments of heat loss by control of the blood flow and capillary contraction are poorly regulated. It is known that nervous subjects and patients suffering from rheumatoid arthritis exhibit an abnormal degree of peripheral vasoconstriction. This explains why rapid cooling, more especially during the passage of active cold fronts accompanied by strong winds causes severe pain in rheumatics or in tissues abnormally sensitive due to

trauma. In the *skin,* cutaneous pains are different. In normal skin, pain results from heating above 43° C or cooling below 10° C, but in some stages of *neuritis* (*i.e.* inflammation of the nerves), pain may be felt even at temperatures just above 30 and below 15° C because arteries are partly blocked and unable to allow the normal increase of blood flow in response to warming. In serious cases it was found that sympathectomy may relieve pain by increasing the blood flow to the affected part. The observation reported by Rentschler *et al.*[2841] is of interest in this connection. A woman suffering from rheumatoid arthritis and severe pain in the upper and lower extremities after every storm, ceased to experience pain in the lower extremities after surgical removal of the second, third and fourth lumbar sympathetic ganglions on both sides of the abdomen. The increased blood supply warmed the lower extremities and restored them almost to normal. The pain in association with storms, however, continued in the arms. Another interesting observation was reported by Mankin to Rentschler *et al.*[2840]. In the U.S. Navy it was observed that men engaged in diving under *high pressure* were relieved from rheumatic pains, which relief continued some time after decompression.

4. Geographical Distribution of Rheumatic Diseases

Various studies (see refs.[2885–2947]) suggest considerable differences in the kind and severity of rheumatic diseases in different countries, but also in the same country. High incidences have been reported from several W. European countries, whereas the incidence seems to be very low among Eskimos in polar regions.

Mills[2883] observed regional differences in *acute rheumatic fever* and *rheumatic heart diseases* in the U.S.A. Acute rheumatic fever is most frequent in the cooler, more stormy parts of the U.S.A. In the tropical and sub-tropical parts with little air turbulence (therefore not in Florida) it is markedly less frequent (10 to 20 times more often in the North than in calm tropical areas). In the North it strikes most frequently in winter and early spring, seldom during summer. In Cincinnati rheumatic fever attacks in March are six times more frequent than in August and September. Nichol[2929] and Paul[2828–2830] found the same relationships for children of the same race with rheumatic heart diseases, the best areas being New Mexico, Arizona and California. Coburn observed in 1931 a rapid recovery of children from New York suffering from rheumatic fever after they had been sent to Porto Rico.

Cobb and Lawrence[2895], comparing the cities of Pittsburgh and Leigh in the U.S.A., observed striking differences in the prevalence rates for *rheuma-*

toid arthritis. Above the age of 55, these are probably 12 per 100 in Leigh against 4 per 100 in Pittsburgh. The difference for rheumatoid arthritis with X-ray changes was even 5 against 0.3 per 100 persons. Although both cities have almost the same annual mean temperature and precipitation, Leigh has a more frequent gentle precipitation against a few torrential rain storms in Pittsburgh. However, undoubtedly racial differences between the cities are also partly responsible for the observed differences. Holbrook and Hill[2775] noticed an improvement in patients suffering from rheumatoid arthritis who were taken to a warm dry climate, *e.g.* South Arizona. Edström [2735 2737] treated rheumatoid patients in air-conditioned climatic chambers with a warm dry atmosphere (32° C, 35% humidity). Four out of seven were cured; two improved but relapsed after they started working; one could not tolerate the indoor climate.

For 26 months Laqueur[2798] studied 738 cases of rheumatic diseases in Ankara (Turkey) and compared the frequencies of the various diagnoses with similar groups in N. Germany. The climate of Ankara is characterized by warm summers and very cold winters (down to —25° C), much sun and a usually dry atmosphere (yearly average 60%; in summer 40%). The daily fluctuations in temperature and cooling are very large. Daily temperature fluctuations of 16° C are common in September. All forms of rheumatism therefore occur in Turkey. There is a very high incidence of acute and chronic polyarthritis (42.5% of the 738 cases) against 19% myalgias (various muscular pains).

A. McKinley[2925a] described the very low incidence of acute polyarthritis in equatorial regions, such as Kenya, Uganda, Nigeria and S.W. Africa. It is more common in Egypt and the Union of S. Africa. In certain parts of India *rheumatic fever* is very frequent, although these areas are located in the Tropics. Cooling conditions may, however, be severe. According to Costedoat and Jeannest[2897a], soldiers in the French army in N. Africa and Indo China suffer less from rheumatic diseases than in France. Studies by Dietrich[2731], using the number of rheumatic complaints per 1000 soldiers in the German army (period 1881–1911) in different parts of the country, showed considerable differences in incidence. Local garrisons were often characterized by very high or very low incidences.

5. *Climatotherapy*

The foregoing summary indicates a number of climatic treatments.

(1) Rheumatic patients should preferably live in *dry, warm, sunny climates* with little air turbulence, not in excessively warm climates causing

considerable perspiration followed by evaporation and cooling. Thalassotherapy is not usually recommended, particularly in cases of acute rheumatism and various forms of myalgia, but swimming in a pool of warm sea water, protected from the wind, may be beneficial for other forms of rheumatism.

(2) *High altitude treatment in climatic chambers* (see p. 640) often strengthens the autonomic nervous system and facilitates a quick vasomotor response during thermal stress. It increases the blood flow in peripheral arteries, the 17-KS secretion by the adrenal gland and so forth. This artificial treatment is usually better than a true high altitude treatment, because considerable cooling may occur at high altitude at certain hours of the day. Also strong ultraviolet radiation has proved to be non-benificial in certain cases of rheumatic diseases. Several reports (*e.g.* by van Neergaard) suggest that polyarthritis in particular is successfully treated at high altitude climate combined with carefully controlled heliotherapy.

(3) Rapid *alternation of very hot and cold towels* applied to the skin of the rheumatic limb (the last treatment being warm), often improves the thermo-regulating mechanism of the skin.

(4) *Warm thermal baths, mud baths, sand baths,* etc., during which the whole body is immersed in warm water, mud or sand of an equal temperature, have a restful effect on a greatly disturbed thermo-regulating mechanism.

(5) In cold climates, local differences in the infra-red radiation of houses, due to damp basements or walls, should be eliminated by putting large electrically heated blankets below the floor covering or against walls, or by having a *double wall and floor heated by air* of constant temperature. Special window constructions should be used to keep out any form of draught. No fireplaces or other chimney opening should be present, particularly in the bedroom and living room, unless they can be hermetically sealed off when not in use.

(6) According to Leiri and others, artificial ionisation affects the degree of rheumatic pain. Little accurate research has been done yet in this field. In this connection the studies of Erban at the Institute of Hygiene in Prague (see *Int. J. Bioclimatol. Biometeorol.,* Vol. III, Part IV, Sect. C6e, 1959) are of particular interest. Exposure for one hour, 3 times a week, for a period of 8 weeks with an air current containing about 4 million ions/ml caused a rise in 17-KS secretion with positively ionised air. Leiri observed increased rheumatic pain with negatively ionised air. If these observations could be confirmed and extended, probably an ionic therapy could be profitably combined with the climatic treatments.

Section 1B. General Pathological Biometeorology (Miscellaneous Meteorotropic Diseases)

So far, only eight important meteorotropic diseases have been discussed. For a number of other diseases similar meteorotropic relationships have been found but considerably less information is available. For this reason the most important weather correlations are only briefly summarised below.

Appendicitis[3005 3014]

Rappert[3012, 3013] studied 1000 cases in 1933. For 20 days the daily number of cases doubled, 16 of which coincided with weather fronts. Maurer[3009], using 1389 cases in Munich (period 1933–1935), observed change in air mass in 78.5% of the cases (normal change in this period was 42.3%). Jaki[3007], using 2185 cases in Debrecen (period 1930–1939), did not observe any meteorotropism in this area. Mills[3009a] observed during heat waves in the U.S.A. (in 1934) an incidence twice the winter values (see p. 517).

Colics[3015–3019].

(1) *Hepatic colics* (caused by gall-bladder stones, cholelithiasis). According to Maurer[3017], 83% of the cases in Munich occur during changes in air mass (normal change 42.3%). According to Hentschel and von Knorr[3016a], particularly common after influx of cold humid air masses.

(2) *Urinary colics* (caused by urinary bladder stones). Hauck[3016], using the n-method (see p. 176), found a highly significant correlation between fronts, or changes in air mass and colics at Leipzig (316 cases on N-day, against 189 on N—1 and 195 on N + 1).

(3) *Renal colics* (caused by kidney stones, nephrolithiasis). According to Maurer[3017] 85% of the cases in Munich occur during changes in air mass (normal chance 42.3%). See also the refs.[3015, 3016, 3019].

Dental caries[3025a–3028d]

The meteorotropic relationships are uncertain. Fries[3027] reported on toothache and weather; Erpf[3026], Lathrop[3028], Mcbeath and Zucker[3028a] noticed seasonal variations in dental caries in the U.S.A., max. incidence in late winter and early spring, minimum in summer. Probably, at least partly, due to seasonal changes in diet and caloric intake, partly due to low Ca and PO_4 level of the bloodserum. According to Sobel[3028d] a diet rich in phosphate increases the phosphate serum level and decreases the cariogenic effect of sugar diet. Hadjimarkos[3027a], East, Blackerby and Dunning observed an inverse relationship between amount of sunshine and caries prevalence rates. According to Anderson *et al.*, Mcbeath and Zucker[3028a] an increase in vitamin D (through ultraviolet radiation or diet) decreases the caries incidence. Schlegel and Warmbt[3028c] observed a statistically significant increase in pains, due to peridontitis and pulpitis, after influx of cold air masses or cold fronts.

Diabetes[3029-3037].

Condition often deteriorating in late autumn and winter; more need for insulin (see also pp. 257 and 286); greater tendency to acidosis and coma (produced by it). According to Henkel[3033], in the period 1927–1931 the distribution of 118 cases of diabetic coma was highest in the period Oct.–April (max. in December and March). This coincides with periods of disturbed carbohydrate metabolism. Similar relationships were observed by Chrometzka[3030] in 1940. Pannhorst and Rieger[3036] studied for 392 male and 327 female diabetics in Germany the month of first onset of diabetes in their life. The females showed a small maximum in autumn, the males a minimum in autumn, steeply rising to December. A further classification of the females according to age and marital status shows different seasonal developments for each group. According to Owens and Mills[3035], diabetes is most common and most severe in middle temperature latitudes and less frequent in tropical regions. Hospital admissions at Cincinnati of 1094 patients (period 1923–1938) indicated that only sclerotic diabetics showed a highly significant increase in admissions during winter, probably due to increased vascular troubles. In non-sclerotic diabetics no seasonal effect was observed.

Morbidity of married females exceeds that of males considerably above the age of 35. In single women the difference is small; diabetes incidence in women with 3–5 children is 3 times higher than in women without children; for those with 6 children it is 5 times as high (in the Netherlands). Among Jews (in Holland) the incidence in males is 2–3 times higher than in gentiles. Genetically latent diabetes seems to be made manifest by pregnancy affecting the pancreas[3037a]. Gerritzen found a 24-h rhythm in sugar secretion and blood sugar level, the amplitude of which increases during periods of increased disturbance of the general metabolism. These various factors affect the amplitude of meteorotropic fluctuations in diabetes in different countries.

Eclampsia[3038-3063]

Convulsive attacks during pregnancy or childbirth marked by high blood pressure, albuminuria, convulsions and coma. Meteorotropic relationships with cold fronts are suggested by a number of studies but not statistically significant. Studies by Jacobs[3050-3052], using 666 cases in Germany, Austria and Switzerland, rather suggest a cold front relationship. The only statistically significant study was carried out by Berg[3039-3041] in Cologne (Germany).

Foehn diseases[3064-3086]

Common in Switzerland, Tyrol (Austria) and S. Bavaria, due to foehn weather (see p. 24), complaints being observed long before obvious changes in weather are noticed (clouds, etc.). Symptoms are migraine; depression of spirits; irritability; dizziness; decreased self-control, reaction speed and production efficiency; increase in suicides and crimes; unfavourable development of various diseases. Storm van Leeuwen[3080-3084] showed that the clinical symptoms are not due to microfluctuations in barometric pressure; Reiter[3076] observed a significant correlation with days when there are considerable disturbances of the electromagnetic long waves (see p. 80).

Goitre[3087-3089]

(a) *Simple goitre,* due to thyroid hyperplasia as a result of iodine deficiency (see p. 268). Meteorotropism related to fluctuations of the iodine content of the thyroid and blood serum (see p. 267); maximum incidence in winter (due to minimum iodine content).

(b) *Exophthalmic goitre* (Basedow's disease), due to hyperthyroidism (see p. 269). Studies by Breitner, Hutter and Jacobowitz *et al.* indicate a minimum in summer, increasing in winter till spring (maximum in May).

Hernia[3102 3103] (*i.e.* abnormal protrusion of an organ or a part thereof)

(a) *Umbilical hernia.* Mori[3102] observed in 1935 in Kyoto (Japan) in 860 3-months-old babies the highest percentage of navel hernia in babies born in January, the lowest incidence in April.

(b) *Lumbar hernia.* Many reports suggest meteorotropism similar to various rheumatic diseases, but no accurate statistical studies have been made so far.

(c) *Inguinal hernia.* Meteorotropism so far not established beyond doubt, but according to Mori[3103] most frequent in babies born in winter, least frequent in April.

Leprosy[3104]

Communicable disease, with predilection for skin and peripheral nerves, caused by *Mycobacterium leprae.* The number of exacerbations during quiet weather conditions seems to be low according to Stein.

*Multiple sclerosis**

Induration with hypertrophy of connective tissue in the brain and spinal cord occurring in scattered patches causing dysfunction of motor movements, paralysis, disappearance of abdominal reflexes, neuralgia of the face

* Extensive literature on multiple sclerosis in relation to environmental conditions was published in *Acta Psychiat. Neurol. Scand.*, Suppl. 147, Vol. 35, 1960 [*Studies in Multiple Sclerosis*, Part 3 (Report on the Geomedical Conference in Copenhagen, 1959), publ. by E. Munksgaard].

nerves, difficulty in speaking, nystagmus (continuous rolling movement of the eyeball), etc. Studies by Allison suggest higher incidence in cold temperate climates and very rare in subtropics (incidence rate in Charleston 13.8/100,000, in Halifax 32.4). In Winnipeg (Canada) 6 times greater incidence than in New Orleans (U.S.A.). The prevalence in cold climates holds for all age groups and both sexes. Studies by Mutlu in Turkey also indicated the highest incidence in coldest regions (particularly above the 40° parallel), very low below 37° parallel. Below the 10° C January isotherm, cases are practically non-existent. Studies by Georgi and Hall in Africa suggest extremely low incidence in various parts of Africa, even in those areas with good medical facilities and therefore trustworthy diagnoses. Acheson, Bachrach and Wright studied 454 war veterans. A regression analysis showed a significant correlation between the average total annual hours of sunshine and of multiple sclerosis. Studies by Fog in the Shetland Islands and Georgi in Switzerland suggest that also trace element deficiency in soil may be an important factor apart from climate.

Pylorospasm[3105, 3106]

Particularly in babies. According to Bayer[3105], most common in winter and spring. Meteorotropism not well established through lack of accurate data.

Rickets[3107–3114] *(rachitis)*

A vitamin D deficiency disease of infancy and childhood with disturbance of the normal process of ossification (the bones becoming crooked and deformed) and decreased metabolism. It is mainly observed between 40° and 60° latitude (common in middle age paintings in Holland, Germany and Flanders, absent in Italy); it is absent in the tropics except in rich families keeping their young children in the darkness; it is common in heavily polluted industrial areas (described by Glisson in England already in 1650); incidence decreases with altitude; in high mountain valleys only observed on the shadow side; according to Schmorl and others, most frequent in winter, decreasing from March, minimum in July-August (see pp. 567 and 583). Hess and Unger[3110] and Huldschinsky demonstrated in 1919 the curing effect of U.V.-light of the wavelengths 302–297 mμ (ultraviolet-B or Dorno radiation, see p. 339). It is essential to prevent rickets (not the duration and quantity of sunlight). It develops vitamin D in the skin (p. 341). Rickets is very rare at very high latitudes. Kestner demonstrated a sudden increase in Dorno radiation in polar areas. Tisdall and Brown[3114a] could demonstrate with young albino rats, fed with a rachitogenic diet, that in Toronto (Canada) a marked increase in the anti-rachitic effect of sunshine occurs on 15 February, *i.e.* at a sun's altitude of 35°. At an elevation of 5300 ft. the critical sun's altitude is 29°.

Skin diseases[2952–2967]

In spring (according to Moro and Mammesheimer) a high incidence of eczema. High incidence in summer of dyshidrosis, miliaria rubra, dermatomycosis, etc. From July–August (often increasing till Nov.–Dec.) higher incidence of furuncles and carbuncles (Klink and Wettstein), erysipelas (Ernst) and erysipeloid (Hindmarsh and Pawlowski). Excessive sunlight causes skin cancer (Mackie), light dermatoses (Blum, Rocha and Silva, etc.), photodynamic diseases, etc. Herpes zoster is (according to Simons) common in the N. hemisphere in July and rare in winter; in Java maximum in April and May, minimum in Jan.–March (wet monsoon).

POSSIBLE MECHANISMS INVOLVED IN METEOROLOGICALLY INDUCED SKIN DISEASES

1. Influence of Solar Radiation

A. Direct influence (this section was prepared by F. P. Ellinger and is a continuation of the section of pp. 338–351)

Since time immemorial man has been aware of the fact that over-exposure to sunlight may produce sunburn (see p. 339). With the advent of the 20th century, it became apparent that sunlight could be a disease-causing (pathogenic) factor. The German dermatologist, Unna[1064], was the first to point to the role of the sun in the induction of skin changes (so-called precancerous dermatoses) in persons who, by occupation as farmers or sailors, constantly exposed their skin to sunlight. Today the *induction of skin cancers by ultraviolet rays* is firmly established (see also pp. 481–490).

Ultraviolet, furthermore, may be the cause of sudden eruption of skin manifestations, usually seen only after considerable exposure of the skin in persons suffering from certain diseases, such as Graves' disease or diabetes. These conditions decrease resistance of the skin to ultraviolet rays due to a variety of factors, such as a change in the blood supply of the skin (number of capillary skin vessels, etc.) (Ellinger[991, p. 635]).

Möller[1039] in 1900 was probably the first to indicate that visible light may play a role in the causation of certain skin diseases. For these diseases, the name "*light-dermatoses*" is in common use. There exists a voluminous literature on light-dermatoses which occur not only in man*, but also in sheep, pigs and cattle**.

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* Detailed descriptions and reference lists may be found in the excellent monographs by Hausmann and Haxthausen[1007], Jausion[1017], Blum[969] and reviews by Stockes *et al.*[1059] and Kesten and Slatkin[1019].

** Note by S. W. Tromp: See also Blum[970] and Rocha e Silva[1015] for details and references. A skin disease of unknown aetiology but affected by sunlight is known as *vitiligo* (characterized by oval or irregular patches of depigmented skin). It is found both in man and in cattle.

An interesting group of, partly photodynamic, light dermatoses is known as *erythema exsudativum multiforme.* It is more common among females than males, particularly blond females; its greatest incidence is in spring and autumn. A recent epidemic of a skin disease in the Netherlands and Germany, resembling erythema exsudativum multiforme, known as "*Planta disease*", is probably due to a sudden introduction of a photodynamic emulsifier in mass-consumed food combined with an increased photosensibility of the general population at the time of the introduction of this food product. (Continued on p. 564)

The role of light in the causation of skin diseases is twofold: it may be an essential factor in their causation, *i.e.*, in the absence of light these skin diseases would not occur; or light may be only an aggravating factor in existing skin diseases.

As the essential cause of light-induced skin diseases, a condition has been recognized which is scientifically designated as "*light sensitization*" (see p. 350).

B. Indirect influence (by S. W. Tromp)

(1) *Increase in sweating and thermal stress.* Heat radiation of the sun increases sweating. A considerable increase in sweating during long periods may cause *dyshidrosis* (an acute recurrent, non-inflammatory vesicular eruption limited to the palms and the soles), which may develop into *dyshidrotic eczema* (red itching skin with small vesicles), *miliaria rubra* (acute inflammation of the sweat-glands with small red papules and vesicles and intense itching and burning of the skin; see also p. 412). Under these conditions a skin disease may develop, due to parasitic fungi, known as *dermatomycosis*.

(2) *Influence of ultraviolet light on growth and development of micro-organisms.*

The lethal effect of U.V. on various micro-organisms on the skin were discussed on p. 518.

2. Decrease in General Resistance of the Body or Increased Development and Spreading of Infectious Micro-organisms and Viruses (see pp. 511–522) *and of the Local Resistance of the Skin to Infectious Agents*

Studies by Marchionini[2964–2967], from which evidence was adduced of the acid coating of the skin as a protective layer against micro-organisms, are particularly important inasmuch as various meteorological factors, such as temperature, humidity and air movement, affecting the sweating rate and evaporation, may influence the growth of micro-organisms on, and their penetration into, the skin.

The formation during summer of *furuncles* (local inflammation of the skin and subcutaneous tissue, due to the penetration of staphylococci into sweat glands, accompanied by local swelling, often also fever, common in neck or axilla) and *carbuncles* (deeply situated, laterally spreading infection, creating multiple adjacent furuncles) is common. They were studied in particular by Wettstein[2967c] and Klink[2962a].

According to Ernst[2959a] *erysipelas* (acute infectious skin disease accompanied by inflammation and redness of the skin, mucous membranes etc., accompanied by high fever, caused by *Streptococcus erysipelatis*) is also a summer disease. The same applies to *erysipeloid* (a skin rash on fingers and hand resembling erysipelas, but no fever, often due to regular contact with infected animal products; infection due to *Erysipelothrix rhusiopathiae*). The meteorotropic relationships were studied by Hindmarsh[2961a] and Pawlowski[2967a].

The favourable effect of high radiation intensity of the sun combined with cooling (great air turbulence and high humidity), as observed along the sea coast, on *skin tuberculosis* (*Lupus vulgaris*) was discussed on p. 504.

Tabes dorsalis[3114b, c]

A slowly progressive, neurosyphilitic disorder, resulting from degeneration of the dorsal columns of the spinal cord and sensory nerve trunks, with disturbances of bones and joints. The lancinating, sharply cutting pains seem to be related to sudden changes in weather (influx of cold polar air, weather fronts etc.) according to Miller[3114c] and Löwenfeld[3114b].

Psoriasis (a chronic skin disease characterized by dry scaly red patches of unknown aetiology) may also be affected by temperature and radiation. It is rare in the tropics. In northern climates the complaints seem to decrease during summer. No improvement is, however, observed if Europeans go to the tropics (according to Simons[2967b]), indicating that racial, nervous or endocrinological factors are more important.

Tetany[3115-3122]

Infant-tetany or *latent spasmophilia* is a syndrome manifested in young children and babies by flexion of wrist and ankle joints, muscle twitchings, cramps and convulsions, due to calcium deficiency with slightly elevated phosphate values of the blood serum, *e.g.* during hypoparathyroidism often occurring together with rickets. In recent years with new prophylaxis very rare. Pronounced incidence peak Jan.–March, very low in summer, autumn and early winter. In Central Europe established by Baar[3115], Behrendt, Cassel, Loos, Escherich, Japha, Moos[3118], Moro[3119-3121] and Siwe[3122], in the U.S.A. by Tisdall, Brown and Kelly. For seasonal changes in phosphate and calcium level of bloodserum see p. 576. They are mainly due to seasonal changes in U.V.-radiation. According to Moro[3119] tetany is common after drastic weather changes (*e.g.* foehn after cold weather). György[3116] also observed tetany, particularly on warm sunny days in early spring. Lassen[3117] observed increased electric sensibility of the peripheral nerves in spasmolytic children during meteorologically disturbed days.

Idiopathic tetany in adults is rare, but according to Frankl-Hochwart also highest incidence in March, low in summer.

Thrombosis and embolism[2968-3004]

The beginning of *thrombosis* (formation of a blood clot within the heart or in a blood vessel) is usually not sharply defined, contrary to *embolism* (the transfer of the thrombus from its point of origin to a distant site causing obstruction). Therefore, only accurate meteorotropic studies are possible with embolism. Despite many studies on post-operative lung-embolism and weather, the results are not very statistically significant. Tivadar[3003], using 156 cases in Budapest, found a significant correlation with fronts. Raettig and Nehls[2992] studied 489 cases in Pommern (Germany). There was a statistically significant correlation with both cold and warm fronts and lightning storms. Reimann and Hunziker[2996] could not confirm a significant front relationship in Basle. On the other hand, Maurer[2990], Kayser[2985, 2986] and Sandritter and Becker[2997] confirmed in different parts of Germany a statistically highly significant correlation between lung embolism and the passage of weather fronts or sudden changes in air mass.

Ulcer[3123-3155]

(1) *Peptic ulcer.* According to Hutter[3134] in Germany, serious complaints are most common in Dec.–February. According to Apperly[3123] in Australia (period 1924–1926) the incidence decreases from Tasmania (40° lat.) to Queensland (25° lat.) and W. Australia (with warm tropical climates).

Einhorn[3130] observed in the U.S.A. a rise in recurrences in the 4th week of Feb. and first week of March, with max. in May; from 4th week in May a decline until 2nd week of June; a gradual rise from 3rd week in Aug. until 2nd week of September (maximum). Scheidter[3151] observed in Bavaria (period 1928–1932) a significant relationship between passages of warm fronts and perforations of peptic ulcers. Gebhardt and Richter[3132], using 1300 cases of peptic and duodenal ulcer in Leipzig (period 1927–1933), showed for peptic ulcer a minimum in April and a maximum in October. Sallstrom[3149] studied 656 cases in Stockholm (period 1937–1942), all established by X-ray diagnosis. A minimum in the number of cases was found in June, a maximum in September. De Franchis[3126] studied 2321 cases of gastro-duodenal ulcer at Bologna (Italy) for the period 1935–1945. The highest incidence was observed during autumn, followed by winter, spring and summer (being lowest). Boles[3124, 3125] analysed all the cases of haemorrhage from gastric and duodenal ulcer admitted at the Philadelphia General Hospital (period 1949–1953). The incidence is highest in Jan., Feb., April, May and June. Schedel *et al.*[3150] studied in Munich (Germany) for the period 1948–1951 the relationship between ulcer perforation and Ungeheuer's weather types (see p. 24). Most perforations occurred during weather phases 3, 4 and 5 (change in air mass), low incidence occurred during phases 1, 2 and 6. A maximum occurred during phase 4, a minimum during phase 6. These correlations are statistically significant. The best correlations occurred with duodenal ulcer.

(2) *Duodenal ulcer.* According to Hutter[3134] in Germany, maximum in May (particularly in men under 40), secondary maximum in November (only in males). According to Einhorn[3130], similar to gastric ulcer. Gebhardt and Richter[3132] observed in Leipzig a minimum in April, maximum in January, with secondary maximum in June–July. Sallstrøm[3149] observed in Stockholm a minimum in June and a maximum in August. Boles[3124, 3125] observed in Philadelphia an increase in the incidence of haemorrhage from duodenal ulcer during Jan., Feb. and March and during Oct., Nov. and Dec.

POSSIBLE MECHANISMS INVOLVED IN METEOROLOGICALLY INDUCED GASTRO-DUODENAL ULCER

Some of the mechanisms involved in the functioning of the stomach and intestines were described on pp. 286 and 288. The following studies contributed to the understanding of meteorotropic gastro-duodenal ulcer.

Studies by Polland (in 1933), Bloomfield *et al.* (in 1940), Roth *et al.* (in 1944), Ihre (in 1948) and Koster *et al.*[3135a] indicate that the amount of free acid in the stomach ranges from the highest to the lowest values as follows: duodenal ulcer, peptic ulcer, normal, cancer of the stomach with free acid, cancer of the stomach with achlorhydria.

The output of acid diminishes with age (Polland[3141b]).

Women with peptic ulceration have a lower level of gastric acidity than men (Perman[3141a]).

According to Koster *et al*[3135a], studying 680 cases of *duodenal ulcer*, 50.2% of the patients belong to blood group O against 38.1% group A (in gastric carcinoma it is the reverse). Buchanan and Highly found in cases of *gastric ulcer* 59% blood group O, 32% group A; Aird *et al.* found 55.4% O and 34.7% A; Clarke 59.6% O, 29% A (these three studies are based on a total of 3700 cases; normal blood group frequencies in Copenhagen 40.6% group O, 44.0% group A). In other words, both groups of ulcer patients are characterized by a *high percentage of O and small percentage of A blood groups*; in gastric carcinoma it is the reverse.

Sundstroem[3154a] and Apperly and Semmens[3123a] noticed in hot tropical areas an *alkalosis in healthy people* due to over-ventilation. It was found that in the blood CO_2 diminished but not the alkali. Experimental production of alkalosis procured considerable diminution of gastric acid. Acidosis raised gastric acidity, which might account for the higher incidence of peptic ulcer in colder climates.

At the Okayama University, Japan, Morinaga[3140] observed in 1955, in 580 cases of gastro-intestinal disorders that the cases of *hyperacidity* increased in winter (41%), decreasing in spring (32%) and summer (28%) and increasing again in autumn (34%). Cases of anacidity decreased in winter and spring but increased in summer. In this connection it is important to realize that winter and summer differ in the tonus of the ortho- and parasympathetic nervous systems. High blood pressures dominate in winter and decrease in summer (see p. 574).

Einhorn[3130] noticed a correlation between *gastro-duodenal recurrences and colds and influenza*, suggesting the meteorotropic effect of cooling. Moynihan[3140a] noticed sudden attacks of gastro-duodenal ulcer after cold showers.

Ellinger[3131] studied, in 1930, the *sensitivity to U.V. light stimulation* in 1200 people in relation to peptic ulcer: (*i*) Persons with an unstable autonomic nervous system (tendency to sweating, tremor, etc.) were 250% more sensitive to U.V.-light than normal persons. (*ii*) In dark haired persons 360% were more sensitive. (*iii*) Blond persons are 50% more sensitive. (*iv*) Normal males are 20% more sensitive than females. (*v*) The light sensitivity is highest in April and October-November; lowest in July. This is particularly pronounced in the group of "autonomic sensitives". (*vi*) The latter group is characterized by a more pronounced erythema after irradiation due to a high degree of histamine production. *Histamine* is a powerful stimulant to the secretion of gastric juice of high acidity and low pepsin content. It is claimed that patients with gastric ulcer respond more markedly. (*vii*) Büchner, Molloy and Siebert[3125a] were able to produce peptic ulcer by histamine injections, which was confirmed by Matsueda[3139a]. (*viii*) Ellinger (see p. 343), Kaufmann[3135a] and Diehl[3127a] observed increased secretion of gastric acidity after U.V.-irradiation.

Studies by Borchardt and Kestner (in 1931) indicate *decreased gastric secretion during heat stress* (decreased appetite). This also explains why there is a tendency to eat spicy food in the tropics. This factor and the gradual adaptation to light stress after May might account for the decreased secretion of gastric acid during June and July.

Patients suffering from *exophthalmic goitre* also suffer most in May. It is known that they have increased sensitivity to light. Ellinger is therefore inclined to believe that the changes in light sensitivity are related to a change in thyroid (and pituitary) function, which in turn would affect the ulcer patients. According to Ellinger three mechanisms may be involved in the thyroid stimulus (*i*) increase in sensibility of the nervous system to histamine; (*ii*) increased cell metabolism in the skin, facilitating the formation of histamine; (*iii*) changes in U.V. absorbing capacity of skin proteins. Either one or a combination of the three processes may be involved. Also a year with little sun and much precipitation during spring and early summer may change the summer adaptation to U.V. light and could increase the light sensitivity in the middle of the summer.

The changes in pituitary function (and pancreas) also affect insulin production, as indicated on pp. 281 and 287. As *increased insulin production* may stimulate gastric acidity, this factor should also be taken into consideration in the study of the meteorotropic mechanism of gastroduodenal ulcer.

The *increase in membrane permeability* (decreased capillary resistance) during heat stress (see p. 335) likewise suggests that during spring perhaps an increased permeability of the gastric membranes facilitates the action of gastric acids. The relation between warm fronts and ulcer perforations (as observed by Scheidter[3151]) and the observation by Schedel *et al.*[3150] that Ungeheuer's weather phase 4 correlates with both the greatest changes in capillary resistance and the maximum incidence of haemorrhages from duodenal ulcer, support this view. Studies by Davis (meteorologist)[3125], using Boles's clinical material, suggest that the greatest number of haemorrhages from duodenal ulcers occur in Philadelphia during periods of great temperature change.

Meteorological factors also probably affect the various physicochemical processes between *intestinal wall and intestinal gases.* Experiments by Schoen[3152, 3153], using dogs' intestines, clarify these meteorotropic processes. Brief mention was made on p. 377 of the experiments conducted by Dexter, Riesser and Kunze, indicating a change in muscle metaboolism and muscle strength during various weather conditions. Parasympathetic stimulation (*e.g.* with pilocarpine) increases the muscular tone. Schoen observed an increased rate of absorption of the gases by the intestinal wall. Atropine (which opposes the parasympathetic action) decreases the muscular tone of the intestinal wall and the absorption decreases, causing accumulation of gases in the intestines. Changes in rate of diffusion through the intestinal wall are also affected by changes in tone of the autonomic nervous system. As meteorological changes affect the autonomic nervous system (see, for example, p. 195), they would, obviously, affect the functioning of the intestines and of the stomach.

High altitude climate probably affects gastro-duodenal ulcers in different ways: increased pulmonary ventilation may cause alkalosis, the metabolic rate is increased (in the initial stages), thyroid activity usually decreases, capillary resistance increases (permeability decreases), parasympathetic stimulation decreases, increased U.V. radiation increases gastric acidity. The latter may account for the high percentage of peptic ulcer reported by Hurtado (see p. 299).

Section 1C. General Pathological Biometeorology (Important Meteorotropic Clinical Phenomena)

In this part of Section 1, a brief summary will be given of a number of, partly meteorotropic, clinical phenomena which may be of interest to the general practitioner.

Subsect. A. BIRTH WEIGHT, BIRTH FREQUENCY, ONSET OF PARTURITION AND SEX

1. *Birth Weight*

Statistical studies in certain areas suggest a seasonal change in the average weight of new-born babies. Abels[3156] was able to show that, after the first world war (period 1920–1922), every year the average weight of new-born babies in Vienna was the greatest in June–July and the smallest in December–March. This applied even more strikingly to the children succeeding the first-born in the same family. Abels' observations were not borne out by the studies pursued at a later date by Hellmuth and Schlossmann in Hamburg, but were corroborated by Peller[3176] and Basse[3177], working in Vienna. The seasonal differences were statistically significant. Katz and König[3166], studying 14,425 new-born babies in Vienna (periods 1910–1912 and 1917–1920), found a similar seasonal change. Also Dulitzky (according to Gerschenson), whose material consisted of 25,388 new-born children, came to the same conclusion. Gerschenson[3162], weighing 12,065 new-born children in the Odessa region (period 1921–1926), found the average weight in the different months to be almost the same, but the number of babies weighing 2500–3000 g were more common in winter, while those weighing 3500–4000 g more common in August–October. As this change in weight occurred in April, before the diet was changed to vegetables, etc., both Dulitzky and Gerschenson believe that increased sunlight is responsible for the seasonal change in weight rather than a change in vitamins. In more recent work Kirsten[3168] reported on the summer maximum in the weight of new-born babies in Norway.

2. *Birth Frequency*

In 1958 Otto[3174] studied the seasonal fluctuations in birth frequency of four groups of new-born babies in Germany for the period 1903–1957 (the war periods 1914–1917, 1940–1945 were excluded), *viz.*, normal, premature, stillborn and deceased new-born babies. The following statistically significant relationships were found: (*i*) *Normal new-born babies*: Maximum number of conceptions (taken as 9 months before the dates of birth) takes place in June (in the case of legitimate children) or in May (in the case of illegitimate children). (*ii*) *Premature babies*: No seasonal fluctuations were observed. (*iii*) *Still-born babies*: Maximum number of births in January; minimum in September. (*iv*) *Deceased new-born babies*: Maximum in February; minimum in September.

In 1950 Reiter[2179] studied the birth frequency of 157,000 new-born babies in Bavaria (Germany) in relation to days of considerable disturbance through electromagnetic long waves (see p. 79). He observed that on such days the birth frequency exceeded the normal expectation by 3.5%. On quiet days the birth frequency decreased by 8%.

3. *Onset of Parturition*

Several reports, *e.g.* by Kuestner[3170] and others[3156, 3182], suggest a relationship in certain areas between weather and the onset of parturition. It has been suggested that warm summers may increase the length of the period of pregnancy. However, so far no accurate statistical studies have been carried out. The influence of weather on *eclampsia* was discussed on p. 560.

4. Sex

According to Petersen[3178], the sex of new-born babies, at least in Chicago, shows a statistically significant *correlation with the weather conditions during the period of conception*, or more specifically with the average atmospheric temperature 285 days prior to birth.

Conceptions taking place during cold periods (and also during periods of extreme heat stress) appear to give a statistical predominance of males, whereas females are more common if the conception took place during warm periods. Petersen assumed that the metabolic state of the maternal body during conception would determine the metabolic conditions of the ovum shortly before fertilization or in the period of rapid differentiation after fertilization. Changes in sperm properties would be less important. As on the average the basal metabolic rate of males in all stages of life is higher than of females (see p. 213), Petersen assumed that an increased metabolic rate of the ovum during fertilization and early stages of differentiation might increase a physico-chemical tendency towards maleness. This assumption is supported by the experiments of Riddle and Fisher described on pp. 265 and 273, indicating a relationship between weather and climate, pituitary function, thyrothropin production and sex ratio. *During periods of increased thyrothropin production an excess of male offspring in pigeons* is observed, even if the diet is kept the same. Similar observations were made by Adler and Whitman in frogs. In this connection the experiments conducted by ten Cate and others (see p. 441) on the influence of temperature on the initial embryonic developments of amphibians, and the observations described on p. 535, indicating a relationship between the month of birth and mental deficiency, are also most instructive.

The quantitative relations between *X chromosomes* (an accessory chromosome both in sperm and ovum being the female determining factor) and *Y-chromosomes* (an accessory chromosome, occurring only in the sperm and being the male determining factor) are known to be mainly responsible for the final outcome of sex. Other environmental factors at the time of fertilization seem nevertheless to play an important part, as has been indicated. This is also suggested by experiments on certain fishes (*e.g. Platypoecilus*) and amphibia, where environmental factors may effect the sex ratio. Work done by Nowinski on the worm *Bonellia viridis* indicated that the larvae may change their sex due to certain extracts from the oviduct in the female worms. Despite these various findings, much more research is required to substantiate Petersen's statistical observations and to clarify the physiological processes involved. Needless to say, if these observations can be confirmed, this whole problem will have far-reaching social implications.

Another interesting seasonal phenomenon in relation to sex was described by Bakwin, Pfaundler[3156a] and De Rudder[6, p. 169]. In summer the *ratio between the number of deaths of male and female babies* (less than 1 month old) changes. It is a known fact that usually more male than female children are born. However, the greater mortality of boys during the early part of life cancels out the male surplus and more or less equalizes the numbers of girls and boys at the age of 18. The number of deceased male babies per 100 female deceased babies, *i.e.* the *mortality sex ratio* of new-born babies *decreases during the summer months*. In other words, relatively speaking, more girls or fewer boys appear to die during the first month of their lives in summer.

Subsect. B. FERTILITY[3183-3187]

The possible influence of sunlight and temperature on the conception rate of horses was discussed on p. 263, while the influence of light on the pituitary and on the production of sex hormones, possibly accounting for differences in sexual activity at different periods of the year, was dealt with on p. 261. Werthessen and Haag (see p. 262) had evidence suggesting that, in horses at least, a low concentration of non-protein sulphhydryl in the seminal fluid is associated with high sperm motility and high fertility and *vice versa*. Above a certain concentration, infertility predominated. Considering the probable influence of sunlight and temperature on the fertility of horses, it seems logical to assume that light and temperature may affect certain organs controlling the sulphhydryl concentration of the seminal fluid. In all probability, the pituitary and adrenal glands are involved. Despite the fact that the detailed mechanisms involved are unknown, a further study of the possible influence of weather and climate on fertility is highly to be desired.

Subsect. C. MORTALITY[3188-3222]

Various aspects of the weather-mortality relationship were discussed on pp. 250–251. The influence of cold and extreme heat stress on heart failure was reviewed on p. 587*, while on p. 499 the influence of weather and climate on respiratory mortality was described. Therefore there seems to be little doubt that weather and climate have a considerable effect on the general death

* In the Netherlands, the total mortality of males in 1948 was 820 per 100,000, of whom 159 died from heart diseases and 136 from cancer, all other diseases (except apoplexy, 61) less than 30 per 100,000.

rate. For the same reason, differences in mortality within the same age group, race and sex can be expected in different countries even if food conditions were the same.

The mortality studies of Boyd[3190], Bundesen and Falk[3191], Cyran and Becker[3192], Kutschenreuter[3209], Ortmann[3212], Spann[3216, 3217], Struppler[3218], Tromp[3221] and others can be summarized as follows:

(1) Mortality increases during the night and reaches a maximum in the early hours of the morning.

(2) The mortality rate is higher in winter than in summer, at all events in N.W. Europe* and the Northern part of the U.S.A. In the U.S.A. this temperature relationship is only observed in persons above the age of 24 and below the age of 1.

(3) Mortality increases during periods of great atmospheric turbulence, the sudden influx of cold polar air masses and the passage of active weather fronts.

(4) Mortality from respiratory diseases increases rapidly during foggy weather with falling temperatures.

(5) Studies by P. Stocks (in 1925) at the University of London, covering October and November of the years 1900–1914 and 1919–1925, indicated a mathematically significant correlation between high barometric pressure and heart failure. However, as in these months there is a significant correlation between temperature and barometric pressure, the correlation found by Stocks does not seem to be a causal one. Studies by Bundesen and Falk[3191] at Chicago, for the period of January 1924 to April 1926 did not confirm Stocks' observation. Heart failure was correlated with low temperatures but may be either directly or inversely correlated with barometric pressure. Considering the influence of fronts and air turbulence, this observation by Bundesen and Falk is not surprising.

(6) In 1950, Reiter[3238–3240] studied the statistical relationships in Bavaria between 52,238 mortality cases and days of great disturbance in electromagnetic long waves (see p. 79). Reiter observed an increase in mortality from 11–30% on such days as compared with quiet days. Males showed a better correlation than females. However, as days of strong disturbances of the electromagnetic field are usually related to other weather changes (fronts, etc.), it seems more likely that the observed correlations are not causal and that the electromagnetic long waves are only characteristic biometeorological indicators.

* Statistical studies in France indicate that general mortality is highest in the period Jan.–March, sharply decreasing in April–June, lowest in July–Sept., increasing in Oct.–Dec (higher than in spring).

Subsect. D. PHANTOM (AMPUTATION) COMPLAINTS[3223–3226]

Although no extensive statistical studies have been carried out, most clinicians agree that patients with amputated limbs often suffer from pain during drastic changes in weather. Reiter and Kampik pulished an extensive report in 1948 on their meteorological studies[3226a]. With very sensitive electronic equipment the muscle potentials in amputated limbs were recorded before, during and after drastic changes in weather (*e.g.* demonstrated by the electromagnetic long waves). During changes in weather, the frequency of these muscle potentials may increase from 200 to more than 1000 c/s, with 0.5 mV amplitude. Similar phenomena, accompanied by pain, were created artificially when the limb was exposed to alternating electromagnetic fields of 50 c/s and 100–200 V. It has been reported by several patients that similar pains occur if they remain some time under tension wires. Apart from direct electrical stimulation, some of the pain is probably due to physiological processes as described on p. 555 in connection with rheumatic pains.

Subsect. E. ELECTRIC FIELD OF THE ATMOSPHERE AND DISEASE[3227–3244]

On p. 455 a brief summary is given of observations suggesting the biological effect of electromagnetic fields on some physiological processes. There are studies that also point to an effect produced by electrostatic fields. For example, Wesley Hicks[3241a] surrounded various plants by a wire screen cage of four-to-the-inch mesh with a charge of 120 V to ground. He noticed in pelargoniums, rhododendrons and beans a stimulation of growth and earlier blooming with positive electrostatic fields, next greatest in negative fields, less for controls and least in grounded cages. The stronger the fields, the greater the growth. As in these experiments only a relatively small number of plants was used and the presence of a charged wire in the open air may have had other physical effects (ionisation, heat radiation effects and so forth) it is not yet certain whether the reported biological effects are really due to electrostatic fields or to other related phenomena. However, as people may be subjected to considerable fluctuations in static fields in the atmosphere for at least part of the day (see p. 74), it is most important that the possible biological effects of electrostatic fields should be studied.

Subsect. F. ATMOSPHERIC PRESSURE AND DISEASE[3245–3259]

On p. 50 it was pointed out that considerable changes in atmospheric pressure may occur during heavy storms. Changes of 40 mm are quite common. The possible effect on water retention and restlessness was mentioned on p. 297. It is therefore not surprising that many studies have been devoted to the problem of the possible influence of changes in atmospheric pressure on disease (see refs.[1319-1333]).

Stähelin[3259], Frankenhauser[3250], Spiro and Mörikofer[3258a], Illénji[3253], Franke and others observed considerable *changes in blood pressure* during periods of rapid barometric fall or rise, accompanied by weather fronts and changing air masses. Recent studies by Betz[1320] and Sarre[1328] in Germany suggest that in this area the blood pressure usually increases during periods of barometric rise. This finding was based on 80 healthy people and a highly significant statistical correlation was found. However, the fact that blood pressure in a healthy population group (as observed by Tromp in the Netherlands) rises both with a falling and a rising barometer but that the rise in blood pressure is always associated with falling temperatures (*e.g.* due to the influx of cold air masses) suggests that the barometric correlation is not a causal one. In certain areas a fall in temperature is correlated with a rise in barometric pressure; in other areas with a fall in pressure. In other words, a change in atmospheric pressure is only a biometeorological indicator of a change in weather, such as changes in air mass, temperature, humidity, air movement, etc.

The assumption that atmospheric pressure has only an indirect effect is supported by the observation made by Alvarez[3245] in Puerto Rico (Caribbean Sea), to the effect that in this area blood pressure increases with sharply falling barometer, whereas in Germany, according to Betz and Sarre, the blood pressure falls with falling atmospheric pressure.

Although small changes in atmospheric pressure in themselves do not seem to cause any clinical phenomena, the studies by Rentschler *et al.*[2841] on barometric pressure and arthritis (see p. 547), the observations by Tromp[2676a] and Krypiakiewicz[2557] on atmospheric pressure and the restlessness of schizophrenics (see p. 537) and the observations by Stocks (see p. 572) on barometric pressure and heart failure, indicate that changes in barometric pressure may nevertheless be important biometeorological indicators of changes in weather which are responsible for various clinical phenomena.

On p. 294 it was pointed out that oxygen stress, due to rapidly falling atmospheric pressure in a climatic chamber, may cause a rise in blood pressure. On the other hand, studies by Jaenisch and Haug[3255] in Königsberg (Germany) suggest that a more complicated process may be involved. The patients, after having rested for half an hour, were placed in a climatic chamber. The atmospheric pressure was gradually reduced to 603 mm Hg in the space of 20 minutes. It was found that both patients with normal blood pressure and hypertonics (without vascular disorders) showed a slight decrease in systolic blood pressure about ten minutes after the pressure reached its lowest point. However, hypertonics with arteriosclerosis showed an increase of systolic blood pressure of 20–30 mm Hg and a diastolic increase of 5–15 mm Hg.

Section 2. Seasonal Pathology

As indicated in the refs.[3260–3392] and on pp. 374–378, many studies have been published on the influence of seasonal changes in weather on various physiological processes, on some properties of the blood and on several diseases.

In De Rudder's well-known book[6, pp. 143–248] an excellent review is given of this whole problem of seasonal pathology. It is for this reason that only the most important results of the study of seasonal pathology will be briefly summarized in Table 39 and 40. Table 39 summarizes the influence of season on the normal physiological processes, whereas Table 40 covers the influence of season on diseases. This latter table is divided into three groups: (*i*) *Pseudo-seasonal phenomena*: infectious and non-infectious diseases which may have a maximum development in certain periods of the year (*e.g.* winter or summer) but not necessarily in the same month each year nor coinciding with the astronomical seasons. (*ii*) *Truly seasonal diseases*, which occur each year almost at the same time and are closely related to changes in weather as a result of the astronomical seasons. (*iii*) *Indirect seasonal effects*. In this group the diseases are mentioned which are indirectly affected by various factors which change during different seasons, such as changes in kind and composition of food (vitamins, trace elements, etc.), changes in clothing, heating and ventilation of rooms, changes in the daily amount of exercise, differences in contact facilities between men (during holidays, in schools, etc.), changes in kind and density of populations of insects causing diseases (either directly or indirectly) and so on. The latter aspect will be discussed on p. 688 by Dr. W. O. Haufe.

TABLE 39

INFLUENCE OF SEASON ON NORMAL PHYSIOLOGICAL PROCESSES

Physiological processes	*Observed seasonal changes*	*Principal authors and references*
Blood		
total protein	Often more than 8.5 g/100 cc serum in winter, less than 7.5 in summer	Tromp[1310]
	Plasma sp. gr. (1.0255–1.0290) is highest in Jan–March	Brown *et al.* (see pp. 374 and 615)

TABLE 39 (continued)

Physiological processes	*Observed seasonal changes*	*Principal authors and references*
albumin	In winter usually > 70%, in summer < 68% (in serum)	Tromp[1310]
γ-globulin	Usually higher in summer (> 13%), lower in winter (< 10%)	Tromp[1310]
haemoglobin	In summer lower than in winter; min. around June	Coulthard[1216], Depner[1218] and Tromp[1310]
leucocytes	High in winter, max. around Dec., min. in Aug.	Lambin and Gerard[1228] and Tromp[1310]
thrombocytes	Max. March-April, min. Aug.	Tromp[1310]
eosinophils	In 1958 in Holland low from May-Sept., high from Nov.-April (min. July-Aug., max. March).	Tromp[1310]
prothrombin	Min. in children (in Hungary) between Sept.-Dec.	Banos[1231]
	In adults min. in winter and spring	Waddell and Lawson[3387a] and Lehmann[3328a]
calcium	Min. in Feb.-March (8.5 mg/100 ml), max. in Aug. (11 mg/100 ml)	Bakwin[3261], Drescher and Kuroda[3324]
magnesium	In Japan min. in Feb. (2.12 mg/100 ml), max. in Dec. (2.85 mg/100 ml)	Kuroda[3324]
phosphate	Min. in Feb., max. in summer and autumn due to increased vit. D. synthesis in the skin by U.V. (average 3-5 mg/100 ml)	Grassheim[1260], Hess[3302] and Williams[1260]
copper	In cows in Holland increasing from 76 μg % (in blood) in Sept. to 104 in May, decreasing again in summer	Van Koetsveld and Boogaerdt[3386]
iodine	In thyroid: min. in Dec.-April, max. in July-Aug. In other organs (in dogs): max. in March. In blood min. in winter 8-9 γ %, in summer 12-15 γ %. Same seasonal fluctuation in cow milk, but rise in blood of men starts before cows leave their stables in spring and change food.	Kendall[3312, 3313], Seidell[3369], Veil[3386b] and Nitzescu[3347]
blood volume	Lower in winter than in summer	Bazett[1244], Bianca[1245], Burton[1246], Forbes[1247] and Maxfield[1248]
packed red cell volume	In Japan max. Feb.-March, min. July-Aug.	Watanabe[1249]
specific gravity red blood cells	Usually rising in summer (in Japan)	Watanabe[1249]

TABLE 39 (continued)

Physiological processes	*Observed seasonal changes*	*Principal authors and references*
oxygen capacity	Increases from Jan.-May (in children < 6 years), from Feb.-Aug. (older children)	Nylin[3348], Straub[3373]
CO_2 capacity	Max. around 21 Dec., min. around 21 June	Nylin[3348], Straub[3373]
blood sedimentation rate	In winter (in Holland) > 60% of healthy male population (age group 30-40 years) a B.S.R. of 1-2 mm, in summer 50 %	Tromp[1310]
bleeding after treatment with anti-coagulants	Max. in Jan.-Feb., min. in July (perhaps due to low prothrombin, low vit. P and K content of the blood and low capillary fragility during winter)	Jordan[1297]
capillary fragility	Highest fragility in children (in Hungary) in March-April, also high in Jan.-Feb., low in July-Dec. (min. in Aug.). High fragility probably due to vit. P. deficiency in winter	Armentano, Rusznyak, Roberts, Zacho, Bicknell, Kerpel-Fronius *et al*[3313a]
cerebral haemorrhage and cephalhaematomata in new-born infants	Highest incidence in winter and spring	Kerpel-Fronius *et al*[3313a], Mc Collum, Hirano, Leppo, Winkler
General metabolism	In *children* max. during autumn. General metabolism sharply decreasing during winter, high during summer. According to Hughes and Sargent[3363, 3364] from April-Sept. a metabolic anaphase, from Oct.-March mainly a cataphase	Chrometzka[1311], Nylin[1315], Fuchs[1312], Hughes[1313], Nitschke[1314]
	During anaphase metabolic demands for reserved substances are diminished and increased in cataphase, *e.g.* in *growing calves* vit. A requirement is greater in winter than summer. According to Mehrotra[3335, 3336] in India cattle and sheep have smaller intake of protein, fats, carbohydrates, calcium, phosphorus and nitrogen in summer than in winter	Sargent[3363, 3364]

TABLE 39 (continued)

Physiological processes	*Observed seasonal changes*	*Principal authors and references*
	In winter twenty percent decrease in metabolism of *rickets patients* due to vit. D shortage (affecting thyroid functioning)	Nitschke[3346]
	The respiratory quotient (*i.e.* the ratio of the volume of CO_2 evolved divided by the volume of CO_2 absorbed in a given time) and the glycogen content of the ventricle tip of isolated, spontaneously beating, *toad hearts* in Australia showed highest average values in January, gradually decreasing till August.	Nayler[3340-3345]
	Human *amino-acid excretion* (*School of Aviat. Med.*, Rep. 59-80, June 1959, Randolph AFB, Texas) shows marked seasonal fluctuations for alanine, arginine, cysteine, glutamic acid, glycine, lysine, serine, creatinine, urea, uric acid and Na/K, in urine of healthy males in Texas, min. in summer (June-Aug.), max. in winter (Feb.-March). For example in case of alanine 0.71 and 1.32 mg/h, arginine 1.48-4.07 mg/h, uric acid 20-40 mg/h, Na/K 2.74-3.01, creatine 106-174	Hale, Ellis and Van Fossan
Blood pressure	In healthy male population in Holland (30-40 years) in winter (Oct.-March) > 60% of male population with diastolic B.P. > 80 mm, in summer < 40%	Tromp[1310]
Ductless glands		
thyroid	Activity and size increase in winter, decrease in summer	Uotila[1354-1358], Cramer[1339] Higgins[1363], Bergfeld[1362] etc.
adrenal gland	17-KS secretion higher in winter than in summer. General activity greater in winter (Sept.-March)	Tromp[1310]
pituitary	Production of growth and gonadotrophic hormones decreasing in winter, increasing in early spring; increased production of thyrotrophin and adrenotrophin in winter	Uotila[1355-1358], Cramer[1339] Higgins[1363], Benoit[1071-1082], Milin[1110], Myerson[838]

TABLE 39 (continued)

Physiological processes	*Observed seasonal changes*	*Principal authors and references*
Gastro-acidity	Hyperacidity high in winter, low in summer, anacidity high in summer	Morinaga[3140]
Growth and weight of children	Slow growth in winter, rapidly increasing in spring; height increase max. in March-May and Nov.-Jan. (in Stockholm). Weight increase in Stockholm max. Sept.-Nov.	Nylin[3348]
Birth weight	New-born babies: greatest in June-July, smallest Dec.-March	Abels[3156], Peller[3176], Katz[3166], Gersehenson[3162]
Birth frequency	Highest number of conceptions in June (legitimate children) or May (illegitimate); stillborn max. in Jan., deceased new-born max. in Feb.	Otto[3174, 3349]
Mortality	In W. Europe max. in Dec.-Jan., min. in July	See p. 571
Acclimatization	Acclimatisation to cold stress in summer more difficult than in winter	See p. 472

TABLE 40

INFLUENCE OF SEASON ON PATHOLOGICAL PROCESSES

Pathological process	*Observed seasonal changes*	*Principal authors and references*
(i) PSEUDO-SEASONAL PHENOMENA		
Non-infectious diseases		
arteriosclerotic heart diseases and apoplexy	Max. in Jan.-Feb., min. in July-Aug.	See p. 507
congenital disorders of the circulatory system (patent ductus arteriosus)	Marked seasonal fluctuation among girls only: max. May-Dec., min. Jan.-April (in Birmingham, acc. to McKeown) or max. Oct.-Jan., min. Feb.-Aug. (in Massachusetts, acc. to Rutstein)	McKeown[3332]
bronchitis	Max. in winter, low in spring and summer	See p. 499
bronchial asthma	Max. in Aug.-Nov. (in the Netherlands)	See p. 467
peptic ulcer	Max. Dec.-Feb., min. June	See p. 565
duodenal ulcer	Max. May and Nov. (only in males)	See p. 566

TABLE 40 (continued)

Pathological process	*Observed seasonal changes*	*Principal authors and references*
appendicitis	Usually more common in warm summers	See p. 559
skin diseases		See pp. 563-564
glaucoma	High in winter (max. in Nov.), low in summer	See pp. 490-494
retinal detachments	Max. in June (Netherlands) or March-May (Switzerland), min. in winter	See p. 494
rheumatic diseases	Usually more common during the cold, humid, windy seasons	See pp. 547-549
diabetes	Coma more common in Dec. and March	See p. 560
goitre (simple)	Max. in winter	See p. 561
goitre (exophthalmic)	Max. in May, min. in summer	See p. 561
mental diseases	Max. unrest in Nov.-Jan.; birth frequency of schizophrenics most common in Jan.-March	See pp. 536-538
	More anencephalics born in Oct.-March (max. Dec.)	McKeown[3331]
Infectious diseases		
tuberculosis	Increased sensitivity to tuberculin test in March-April, low sensitivity during autumn; mortality increases in spring	See pp. 503-504
scarlatina	Max. end Oct.- beginning of Nov.; increasing from August-Nov. (max.)	See p. 524
diphtheria	Max. Nov.-beginning of Dec.; increasing from August - Nov. (max.)	See pp. 523, 527
common cold	Max. in Feb.-March; increasing from Sept.-March	See pp. 523, 526
influenza	Max. in Dec.-Feb.; increasing from Sept.-March	See pp. 523, 528
lobar pneumonia	Max. in Dec.-Feb.; increasing from Sept.-March	See p. 524
epidemic cerebrospinal meningitis	Max. Dec.-April; increasing from Sept. -March	See pp. 524, 533
variola	Max. in March; increasing from Sept.-March	See p. 524
(ii) TRULY SEASONAL PHENOMENA		
Non-infectious diseases		
hay-fever	Usually May-June	See p. 463

TABLE 40 (continued)

Pathological process	*Observed seasonal changes*	*Principal authors and references*
rickets	Most frequent in winter due to vitamin D deficiency, min. July-Aug.	See p. 562
infant tetany	Max. Jan.-March	See p. 565
Infectious diseases		
diplobacillus conjunctivitis	Max. in July	See p. 496
cholera	Max. in Aug.; increasing from May-Sept.	See p. 523
typhoid fever	Max. in Aug.; increasing from May-Sept.	See p. 524
poliomyelitis anterior acuta	Max. in Aug.-Sept.; increasing from May-Sept.	See pp. 524-530
bacillary dysentery	Max. in summer; increasing from May-Sept.	See p. 523
(iii) INDIRECT SEASONAL EFFECTS		
*Vitamins** (footnote see p. 583)		
vitamin A and carotene (in the body converted into vit. A)	In the Netherlands and Belgium in winter 1–5 γ/100 cc milk, in summer 25-30 γ	Van Wijngaarden and Deco[3276]
	In England in cows serum vit. A values during pasture feeding (April-Oct.) 1.35 mg/100 ml, during stall feeding (Dec.-April) 0.23 mg. In butter-fat resp. 18-27 I.U./g of fat (in Aug.) against 16-11 (in April)	Lord[3330]
	According to Cunningham *et al.* and Buls *et al.*, in Australia, in various fish varieties increased vit. A content of liver (and decreased fat content) during winter months (May-Aug.).	Van der Rijst[3379-3385]
vitamin B	Seasonal wave of *pellagra*, max. in May-July. According to Sargent this peak cannot be explained solely in terms of dietary deficiencies; probably seasonal variation in metabolism is a significant factor. The influence of temperature, light intensity and daily number of sun hours on the vit. B_1 (thiamine) content of plants was discussed on p. 348.	Sargent[3365]

TABLE 40 (continued)

Pathological process	*Observed seasonal changes*	*Principal authors and references*
vitamin C (ascorbic acid)	Content varies considerably in different plants and even in the same organs; greatest concentration in green parts and in the skin of fruits. Vit. C content related to growth and chlorophyll content of plants; it increases till flowering stage followed by a decrease	Van der Rijst[3379-3385]
	In potatoes decreasing from autumn till spring. Suddenly increasing in June and July. Same observed by Dietz in germinating oats and barley	Van der Rijst[3379-3385]
	Summer cabbage contains 50% more vit. C than winter var. (Gould); young potatoes are richer in vit. C than late growing varieties (Nehring): spinach collected in autumn has 20-25 more vit. C than if collected in spring (Tressler and Mack); fruits or beans collected from the same tree or plant become poorer in vit. C the later the fruits or beans are formed (Mack and Tapley); red and black berries and strawberries are poorer in vit. C at the end of the growing season (Olliver)	
	According to Rohmer *et al.* and Stoerr average vit. C content of milk in Jan.-Feb. 0.8, March-May 1.2-2.7, Aug. 1.6-2.3, Oct.-Nov. 2.5-3.0 mg% irrespective of the food used.	Van der Rijst[3379-3385]
	General resistance and adaptation to cold stress depend on vit. C level received daily and the level in tissues, especially the adrenals. Adrenals retain more during cold stress (less secreted in urine) until animals become acclimatized.	Dugal and Thérien[615]
	In Paris, in June-July, low vit. C content of human blood plasma (usually < 2 mg/l plasma), in Sept.-Oct. increasing to 6-14 mg	Raoul *et al.*[3385]
	Max. incidence of *scurvy* in May-Aug.	Sargent[3364]
vitamin D	In Michigan (U.S.A.) in cow milk max. in July, Aug. or Sept. (up to 44 U.S.P. units per quart of milk of	Bechtel and Hoppert[3264]

TABLE 40 (continued)

Pathological process	*Observed seasonal changes*	*Principal authors and references*
	Guernsy cows), min. around Feb. (5 U.S.P. Units). Close correlation found between antirachitic potency of milk and amount of sunshine to which the cows were exposed	
	Summer butter contains 2 to 3 times more vit. D than winter butter (the changes occur before the cows switch over from stall to pasture feeding). In certain years there is a difference of 9 to 1. The increase is partly due to increased sunshine on cows, partly due to greater vit. D content of grass in summer. Artificial irradiation of the udder of cows with U.V. usually increases the vit. D content of the milk produced	Campion, Henry, Kon and Mc Cosh (See Van der Rijst[3379–3385])
	Vit. D supply inhibits hibernation in animals, body temperature remains normal, *i.e.* it stimulates general metabolism and thyroid functioning (see also pp. 264 and 567). Rickets in rats causes a 20% decrease in general metabolism, disappearing after vit. D supply (see p. 562) or U.V. irradiation	Nitschke[3346]
vitamin K	Max. deficiency in winter; at least partly responsible for low prothrombin serum level in winter and high incidence of cerebral haemorrhage in new-born infants in winter	Kerpel-Fronius *et al.*[3313a]
Trace elements		
calcium, phosphorus, magnesium, nitrogen and potassium	Apples (in Washington) showed lowest concentrations of phosphorus, magnesium and calcium at the end of the growing season, whereas nitrogen and potassium were present in greater quantities than during the early season	Rogers and Batjer[3360]

* To illustrate the important role of vitamins in the living organism, a short summary of a number of interesting data is given.

Clinical effects of vitamin deficiency

Vitamin A. Inhibiting growth; sexual maturity being delayed and ovulation infrequent (in rats); lacrymal glands cease to produce tears; corneal epithelium becomes thickened, dry and wrinkled; salivary glands do not secrete in the alimentary canal; lining cells of upper respiratory tract become keratinized; reduction in local resistance to infection is due to changes in epithelia; thyrothropin production and thyroid activity increased (see p. 264).

Vitamin B complex (B_1, B_2, B_6, *etc.*). Essential for metabolism; thiamine deficiency affects various subjective nervous manifestations (irritation, depression, etc.), beriberi disease, pellagra.

Vitamin C. Skin becomes rough and dry or shows petechial haemorrhages; slow wound healing; decreased physical efficiency; scurvy, changes in teeth; vitamin C increases stimulation of thyroid with thyrothropin (see p. 264) and increases activity of the adrenal gland and adaptation to cold stress (see p. 279).

Vitamin D. Deficiency inhibits calcium and phosphate absorption from the intestine, and normal calcification of bone causing rickets. Supply inhibits hibernation of animals (according to Nitschke) and stimulates thyroid functioning.

Vitamin E. In rats atrophy of seminiferous tubules; inhibiting foetal growth; it may cause muscular dystrophy. Surplus may improve muscular performance (decreasing oxygen requirements) and reduces the number of malformations in rabbits born under conditions of oxygen starvation (see p. 296).

Vitamin K. It maintains normal level of plasmaprothrombin and normal coagulability of blood (see p. 318). Deficiency causes cerebral haemorrhage in new-born infants, increased bleeding after anti-coagulant treatment.

Vitamin P. Deficiency lowers capillary fragility (according to Armentano, Zacho, Bicknell and others).

Distribution of vitamins in different animal organs (see refs.[3379–3385])

Vitamin A. Cow liver: 8400 γ/100 g, cow kidney: 180 γ/100 g, cow meat: 22 γ/100 g (according to Droese and Bramsel). Rabbit liver: 11,000 γ/100 g, rabbit kidney: 100 γ/100 g (according to Edisbury *et al.*).

Vitamin B_1. Cow heart: 675 γ/100 g, cow liver 460 γ/100 g, cow kidney: 316 γ/100 g, cow meat: 170 γ/100 g (according to Droese and Bramsel).

Influence of sex on vitamin content

In organs of many female mammalia usually a higher vitamin content than in males.

Influence of age on vitamin content

Vitamin A content of the liver increases with age. This is particularly true in fish.

Influence of weather on vitamin content

In general, meteorological factors increasing the growth of plants also increase the vit. C and carotene content of these plants, which also explains differences in vit. C content of food from one year to another. It may well be that this affects the functioning of the adrenal gland (see p. 279) man and the general resistance of the population to infections (see p. 516).

(1) *Influence of humidity.* Experiments by Hoffman, Kraus and Washburn (in 1937) in hot-houses, indicate that vit. C content of tomatoes decreases with little water supply. Increase in water increases vit. C till a maximum is reached. Also various grasses show a decrease in vit. C during periods of drought (*e.g.* in W. Europe often in May), which increases after a period of rainfall. On the other hand, according to Wasicky, heavy rainfall during several hours in succession may reduce the vit. C content of plants with 34–70% (at least at Sao Paulo).

(2) *Influence of light.* Exper ments by Moldtmann in 1939 demonstrated a decrease in vit. C content of plants with decreasing light intensity. For example, oats in the open air contained 68 mg%, under glass 47, in darkness 29. Other research workers confirmed this observation. A concomitant of decreasing light intensity, however, appears to be an increased vit. C content of certain plants, such as onions. Studies by Borthwick and Hendricks in the U.S.A. suggest that these processes are related to certain enzymes sensitive to particular parts of the solar spectrum.

(3) *Influence of temperature.* In darkness, some plants show an increase in vit. C at low temperatures (*e.g.* 3° C), others at higher temperatures and certain plants do not seem to be affected by temperature at all[3379–3385].

(4) *Indirect influence of weather through changes in acidity of soil.* As precipitation, temperature hours of sunshine and wind speed greatly affect the pH of soil and as the maximum amount of vit. A and vit. C occurs during optimum growth of the plants, which greatly depends on an optimum pH (different for each plant), the obvious inference is that weather may also affect the vitamin content of plants in an indirect way.

Section 3. The Influence of Weather, Climate and Season on the Effect of Pharmacological Treatment

by
S. RENAUD
(Subsect. A by S. W. TROMP)

Subsect. A. INTRODUCTION

Various authors, Findeisen[3401], Macht[3408], Nedzel[3410], Ossoinig[3412], Petersen[3413], Sargent[3415], Marshall and others (see also p. 514), have pointed out that the same chemical substance (in the same concentration) administered to a healthy person or patient may act entirely differently under different weather or climatic conditions, contrary to the general belief of most clinicians. This observation is most important from a practical point of view because it suggests that the same substance may be beneficial in a particular period and toxic in another. Needless to say, if these observations were confirmed, both the physician prescribing drugs and the pharmacist preparing them, would have to bear this phenomenon constantly in mind. But it is not only differences in the toxicity of a certain drug at times of the year that are important. The same drug administered in various countries having different climatic and weather conditions may be expected to have entirely different results; indeed, this may even account for certain contradictory reports made by physicians in various parts of the world who, applying the same drug, obtained different results. The study of *geographical* and *biometeorological pharmacology* may prove to be an important field of study in the future.

The differences in therapeutic and toxic action of a drug could well be the result of a number of such factors as: (*i*) The *influence of the physico-chemical condition of the patient,* depending on race, sex, age, general health and psychological stress condition and on environmental conditions (such as climate and weather) affecting the physiological processes of the body; (*ii*) The *influence of the dosage, method of preparation, the form in which a drug is administered and environmental factors* (such as temperature, humidity, radiation) affecting the physico-chemical properties of the drug itself; (*iii*) *The influence of the time factor, i.e.* how long and how frequently the drug is administered; (*iv*) *The influence of other drugs* administered at the same time.

These various conditions affecting the therapeutic and toxic action of drugs suggest that, even on theoretical grounds, changes in weather and climate throughout the seasons, due to changes in temperature, air turbulence, solar radiation (total energy and composition of sun spectrum), etc., could be expected to influence the specific action of drugs and their degree of toxicity. This theoretical assumption is supported by the observations described on pp. 514–517, indicating that, even in a healthy person, the local and general resistance to infections, changes as a result of meteorological conditions. Therefore, the quantities of a drug required to suppress an infection will also change. These theoretical considerations are supported by the following experiments.

Experiments with digitalis

Between 1927 and 1934 Macht *et al.*[3108] studied the possible correlations between specific meteorological factors and drug action in the Pharmacological Research Lab. (Hynson, WestCott and Dunning) at Baltimore, Md. (U.S.A.). In particular, the difference in toxicity of digitalis (an important heart drug) was studied by using biological methods (Hatcher-Brodie cat Method*).

It was noticed by Macht and his assistants that pronounced differences in toxicity occur under different weather conditions. In particular great changes in barometric pressure and humidity seem to correlate with these pharmacological changes. For example, a particular tincture of digitalis became more toxic during a severe storm with rapidly falling barometric pressure than during periods of high atmospheric pressure; in other words, less digitalis tincture per kiloweight is required to kill a cat during stormy weather than during quiet weather conditions.

It has been stressed many times in the previous chapters that in all probability barometric fall as such (at least within certain limits) has no or little biological effects, but usually coincides with various other important changes in meteorological conditions, such as temperature. However, according to Macht, the same results were obtained in the mountains during quiet weather (lethal dose at Baltimore in August 1927 was 10.6 ml, the same tincture in the Blue Ridge Mountains was 8.0 ml), which may suggest a true barometric effect (see p. 293). A particular digitalis tincture was tried by Macht on 3rd July 1933 on a quiet day (B.P. 795, R.H. 70%), on 23rd August 1933 during a severe tropical storm at Baltimore (B.P. 745 mm, R.H. 76%) and on 29th August 1933, after the storm had passed and conditions had returned to normal (B.P. 766 mm, R.H. 65%). The amounts of diluted tincture required were 10, 7.84 and 11.4 ml respectively. During a heavy rain storm on 16th April 1929 a tincture which was normally found to have a killing

* The quantity of tincture of digitalis, diluted 1 : 10 with physiological saline (*i.e.* solution of 0.9% NaCl), required to kill a cat when injected at regular intervals into the femoral vein, the animal being under ether anesthesia. The quantity of the tincture divided by the weight of the animal gives the lethal dose in "cat units".

power of 13.4 ml, decreased to 10.5 ml. According to Macht, the same results were obtained time and again during 7 years of observation, which suggests that important weather changes affect the action of drugs. This observation is also supported by the various observations mentioned on pp. 514, indicating considerable changes in the physico-chemical state of the blood as a result of weather and climate.

The *high altitude effect* observed by Macht was confirmed in 1928 in the Austrian Alps by Jarisch (Head of the Pharmacological Laboratory of the University of Innsbruck) and in 1932 by Lehman and Hanzlik[3107] (Dept. of Pharmacology, Stanford University School of Medicine, San Francisco, U.S.A.). In all these experiments there was no question of deterioration of the drug itself, as was proved by simultaneous trials at sea level. Lehman and Hanzlik studied the effect of high altitude on the emetic and fatal doses of digitalis in pigeons and cats[3107]. The same tincture was used at different altitudes: in San Francisco at sea level (B.P. 760 mm) and at Tioga Pass in the Sierra Nevada mountains, California at 3000 m (B.P. 526 mm). A total of 288 emetic tests with 6 doses of digitalis, ranging from 5 to 30 mg/kg body weight, were made in 144 different pigeons. Except for the 5 mg dose, a considerably higher percentage of vomiting occurred at Tioga Pass with the same dose of tincture. For example, with the 15 mg dose 29% emesis occurred in San Francisco as against 63% at Tioga Pass.

This means to say that the emetic potency is considerably greater at high altitudes. The fatal dose of digitalis, determined in 74 pigeons, proved to be 90 mg. in the mountains (20% mortality) whereas this dose was not lethal in S. Francisco (mortality 0%). With 105 mg at S. Francisco the mortality was still 0, against 67% at Tioga Pass. At 120 mg the ratio was 40% in S. Francisco against 80% at Tioga Pass. Here was another demonstration of the increased toxicity of a drug at high altitudes.

Whereas it is easy to see that *the effect of a heart drug may be greater at high altitudes,* the fact, demonstrated by Macht, that *a drop in barometric pressure during stormy weather can have a similar effect* was not hitherto known.

Experiments with tuberculin

Several years before the publication of Macht's paper, similar observations were described by Ossoinig[3412]. It was already known that the effect of tuberculin varied considerably as a result of other diseases; *e.g.* decreased sensitivity during measles. However, Hamburger[3406] reported a greater sensitivity in spring (March–April) than in autumn. Peyrers made a similar observation in 1920 with the Pirquet reaction in 150 patients, the cutaneous sensitivity being stronger in the period Dec.–July than from August–Nov.

Ossoinig found in 300 patients an increased sensitivity from March–August 1923, but in 1922 no correlation was found. Nevertheless, in 1922, 1923 and 1924 a slightly increased sensitivity was observed in March and April.

For the years 1921–1924 the daily fluctuations in tuberculin sensitivity of 10 patients was studied by Ossoinig. An increase usually lasted one week only, a decrease 1–3 weeks (up to 8 weeks). All the same, steep increases on the same day were also observed in a number of patients despite of the fact that each patient had a different daily dose. Such increases could not be explained by a deterioration in the condition of the patients or by other obvious reasons. Studies by Heuss seem to suggest that these daily changes are related to the passage of weather fronts. The increased sensitivity in spring was also confirmed by Karczag and Arnfinsen.

Experiments with atropine

Hamburger[3406] described how, in his clinic, children required on certain days a considerably larger dose of atropine than usual (sometimes twice the normal value) before a reaction occurred; a fact likewise observed by Ritte.

Experiments with morphine

In 1937 Nedzel (Dept. of Pathology and Bacteriology of the University of Illinois, U.S.A.) was able to demonstrate[3410, 3411] the appreciable effect of meteorological disturbances on mortality from morphine sulphate in 1350 mice of approximately the same age, living on normal, acid and alkaline diets respectively. During so-called *pressor episodes* (a collective term used by Petersen, Sargent and others to define numerous physiological changes occurring coincident with or following the cold front) Nedzel noticed that the minimal lethal dose of morphine caused an increase in the total death rate of mice. The mortality rate was affected by the acidity and alkalinity of the diet.

Sargent[3415] continued these studies *in relation to cold fronts*. Mice living on normal, acid and alkaline diets were injected with a fixed quantity of morphine sulphate. The time interval till death occurred and the percentage of dying animals were regularly recorded. The following observations were made: (*i*) Meteorological conditions vary the toxicity of morphine sulphate. (*ii*) The lowest mortality rates were observed on days of stable meteorological conditions. (*iii*) If a cold front closely precedes the injection of morphine sulphate, the toxicity is at a maximum both for normal and for acid and alkaline diet groups. (*iv*) If the cold front passes some time before the injection, the toxicity is low. (*v*) According to Nedzel, during the passage of cold fronts the death rate in alkaline-diet groups is slightly higher than in the acid group. However, after the cold front has passed, the death rate is highest in mice on normal and acid diets. Mortality is low in the mice living on alkaline diets. Sargent explains this by the fact that tissue acidity increases to such an extent during pressor periods that acid food has an unfavourable effect, whereas alkaline diets have a neutralizing influence.

Experiments with colloidal fluids

In 1939 B. Düll and T. Düll[3404, p. 133] put forward an hypothesis on the possible effect of electric disturbances of the atmosphere on the stability of colloidal fluids. It was known to them that certain proteins and positively charged inorganic colloids coagulate under the influence of β- and γ-radiation. Several reports have been published on coagulation phenomena in milk during thunderstorms, which could not be explained by bacterial action, and which, according to Van Hettinga, are due to changes in redox and surface potentials of the colloid as a result of strong disturbances in the atmospheric electric field. In the paper industry similar reports describe the effect of lightning storms on paper glue. Considering the various weather phenomena described in previous pages, we suggest that rapid temperature-humidity, rather than electrical, changes during thunderstorms are responsible for these colloidal reactions. However, the Düills' observations formed the basis of further studies by Findeisen.

In 1943 Findeisen[3405] studied the influence of weather on a 0.8% *colloidal solution of arsenic trisulphide* on a very large scale. Inspite of a number of minor technical inaccuracies in the daily preparation of the colloids, the same reproducible chemical reactions were obtained during quiet weather. The condition of the colloid was determined by measuring the electrical conductivity in a number of samples of the same colloid which were placed in closed glass containers in different localities of Bavaria, at Oberstdorf (elevation 810 m) and at the Nebelhorn (1932 m elevation). The containers were placed in heat-insulated wooden boxes. Temperatures of the fluid and conductivity were automatically recorded three times a day at 7, 14 and 21 hours. For further details see ref.[3405]. As a result of a statistical analysis of 35,000 automatic recordings during 339 days, the following conclusions were drawn by Findeisen: (*i*) The colloid shows a daily rhythm both at Oberstdorf and Nebelhorn, apart from a gradual decrease in resistivity with increasing age. Highest values occur between 2 and 8 hours; lowest values between 14 and 20 hours. (*ii*) Screening the containers against external electromagnetic waves did not affect the observed resistivity values. (*iii*) No relationship was found between solar activity and changes in colloid resistivity. (*iv*) Differences in cloudiness do not affect the results. (*v*) During rainy weather and lightning storms, the ageing rate of the colloid is retarded (resistivity too high); during foehn conditions, ageing is accelerated (the resistivity is relatively too low). (*vi*) When a cold front is approaching (following a foehn influx), the sol resistivity decreases rapidly and reaches a minimum during the passage of the cold front. Immediately afterwards, the resistivity begins to rise again.

As these cold fronts in Bavaria coincided with a steady drop in barometric pressure, Findeisen assumed that a certain barometric effect was one possible cause of these colloidal changes.

In his excellent report on a number of places he mentioned that temperature insulation, despite precautionary measures, was not ideal. Undoubtedly larger fluctuations were excluded, but the small temperature changes which are common during the passing of a foehn or cold front, were not eliminated.

In Part II we dealt at large with the necessity of registering biometeorological temperature changes *i.e.,* the actual cooling factor. The fact that resistivity changes in the cellar are smaller than near windows on the first floor is a pointer. Although no conclusive explanation is at hand as yet, the most important datum emerging from this extensive study is the observed fact that even inorganic colloids are affected by sudden weather changes, either as a result of differences in cooling effect (temperature-humidity-wind-speed factor), or other unknown factors (but in all probability not electro-magnetic waves). There is every reason to assume that also the organic colloids in the surface tissues of the human body are affected by these weather changes, which may explain certain aspects of meteorotropism.

Experiments with single biological systems

Similar enlightening studies were carried out by Pichotka[3414], Professor of Physiology at the University of Berlin, who studied the influence of weather on single biological systems, such as potatoes or potato sections. Pichotka, using a Warburg apparatus, observed the hourly changes in metabolism of potato sections as a function of temperature for periods of 6 days. A total of 4500 observations was collected. It was found that, if a potato section was subjected to a constant temperature (between 15 and 30° C), a steep rise in metabolism for 12–24 hours was followed by a gradual fall until a fairly constant level was reached after about 2 days. This is true for each of the temperatures between 15 and 30° C, but, the higher the environmental temperature is, the steeper are the rise and subsequent fall in metabolism. The same applies to other external stimuli. The observed mechanism suggests that pharmacological treatment, particularly of external parts of the human body, may have different effects on tissues under different weather conditions as a result of differences in cooling power of the environment.

Experiments with urine

On p. 540 the experiments of Fischer were briefly described, indicating that the difference in toxicity of the urine of schizophrenics and normal persons practically disappears on days of drastic weather changes as a result of the passage of weather fronts.

Experiments with hormones

Studies in recent years by Selye and his collaborators in the "Institut de Médecine et de Chirurgie expérimentales" at the University of Montreal (Canada) have revealed the great importance of various stress conditions on the result of pharmacological treatments. Considerable evidence is adduced to show that hypersecretion of adrenocorticotropic hormones and adrenocortical steroids and the release of anti-diuretic hormone play an important role in this stress mechanism. The great influence of weather and climate on the secretion of these various hormones was discussed at length on pp. 256-283.

Selye and his collaborators also showed that stress affects the permeability of various membranes of the body and that therefore certain drugs can enter the blood stream more easily. Various experiments indicating the influence of weather changes on the permeability and capillary resistance of membranes are described on p. 335. It seems logical therefore to assume that weather and climatic stress like other forms of stress, affect the action of drugs.

Subsect. B. EFFECT OF STRESS ON ABSORPTION, PHYSIOLOGICAL ACTION AND TOXICITY OF DRUGS*

by

S. RENAUD

1. *Introduction*

It is well known that the pharmacological action of certain drugs is considerably modified by pathological conditions. Chloroform anesthesia, for example, is definitely contraindicated in patients with hepatic diseases. Therapeutic doses of diuretics produce only a slight augmentation in the urine flow of a normal individual, but may promote the excretion of several liters of fluid in an edematous patient. Myxoedematous subjects may be

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seriously narcotized by a dose of morphine normally only moderately depressant. Certain of these modifications by adverse conditions are more or less due to the specific action of the condition, as is the case of the dramatic effect of chloroform, an agent hepatotoxic in itself, in patients already suffering from hepatic disease. But when the same change in the pharmacologic action of a drug is seen after such diverse conditions as severe illness, surgery, trauma, extensive burns and exposure to cold, it is no longer a specific effect of one particular condition. All these agents induce a similar pattern of changes in the subject, changes that are the result of the subject's response to the injury, or insult, and have been named the "alarm reaction"[3489] and the stress response. The magnitude of this stress response can be measured by several tests, as has been shown in burned patients[3138] or in soldiers wounded in the Korean war[3449].

The concept of stress itself being only recent[3490], it is not surprising that its effects on pharmacologic treatments have not yet been generally recognised and systematically investigated. The first general report on stress[3493] revealed the existence of a few papers on the influence of stress in pharmacology scattered throughout the literature, but even now it seems that no correlative knowledge on the subject is available. This is mainly due to the fact that most of the papers deal with the effect of a particular adverse condition on a certain drug: only correlations of the different experiments in this field can shed light on the nonspecific mechanism involved.

The mechanism by which stress exerts its effects can be briefly summarized as follows: it seems reasonable to assume that hypersecretion of adrenocorticotrophic hormone and adrenocortical steroids are involved[3430,3492]. But the adrenal cortex does not appear to be directly responsible for the changes, and corticoids may be considered as necessary but not the cause of certain of the alterations observed after stress[3450–3453]. Other mechanisms such as the release of anti-diuretic hormone[3471,3484] are also involved in the stress reaction, but it is not within the scope of this paper to examine all of them. For this purpose, the reader is referred to Selye's excellent review on the subject[3494].

As the main object of this paper, the known facts regarding the action of various stressor agents on certain pharmacologic treatments will be summarized. Since drugs can be affected by various ways, it is proposed to examine separately (*i*) The action of stress on the absorption; (*ii*) The physiologic effects, and (*iii*) the toxicity of drugs. Although we feel that this division is somehow artificial, the different phenomena being closely related, it is, nevertheless, retained for the sake of clarity. In each case, in view to illustrate these stress effects, a few striking examples have been selected.

2. *Effect of Stress on Drug Absorption*

Water and electrolytes

Recently it was claimed[3448] that soldiers suffering from various injuries in the Korean war, and therefore under considerable stress[3449], presented an impaired water absorption from the gastro-intestinal tract; this had also been shown in dogs submitted to acute hemorrhage[3442].

Prior to the discovery of stress it was demonstrated[3463] that the disappearance time of intradermally injected sodium chloride solution was reduced in several pathologic conditions. This procedure was even considered as a test of the "resistance of the terrain" that may help the physician in the treatment of the patient or to determine the operability of old or debilitated individuals. This shortening of the disappearance time was seen in patients with scarlet fever or diphtheria[3419, 3462], lobar pneumonia[3444], toxemia of pregnancy[3458], cardiac diseases[3476], thyrotoxicosis[3473], jaundice[3474], tuberculosis[3440], the extent of shortening being roughly proportional to the severity of the illness. The same modification in the rate of absorption was seen when sodium chloride was injected, this time subcutaneously, in shock patients[3457]. It was shown that physiologic saline was absorbed more quickly from the small intestine in dogs submitted to anoxic anoxia[3499, 3500], or after controlled bleeding[3501], than in the control animals, while other authors[3442] claimed that this absorption is not clearly affected until the advanced stage of shock is reached.

Experiments undertaken with phosphate salts in guinea pigs[3475] demonstrated that the stress of trauma or of evisceration was able to bring a clear diminution in the intestinal absorption of these salts.

Glucose

Continuous exposure of rats to certain damaging agents, such as cold, exercise, various drugs, X-rays, was shown to induce a marked increase in the hyperglycemic action of orally administered glucose[3468]. The same striking elevation in the blood sugar concentration was seen to follow various types of injuries[3448] and in patients with neoplastic diseases[3465, 3466]. Therefore, the changes in the response to these agents cannot be regarded as specific pharmacologic actions, but could be the result of the stress damaging effect of such agents. From these experiments it is logical to conclude that stress markedly increases the absorption rate of glucose, as is indicated by elevations in the blood sugar concentration. But the results obtained by testing the absorption of glucose with this method do not give definite proof of a greater absorption of this sugar. In fact, other investigators found that by determining the absorption of glucose directly in the intestine, the stress of acute hemorrhage or trauma either did not effect[3501] or lowered[3433, 3442] the animal's absorptive capacity for glucose. These last findings are not, as it would appear, in opposition to our concept of the stress effect on glucose metabolism, but are in accordance with the well known fact that the stress induced discharge of excess glucocorticoids and adrenaline affects the glycemia mainly by increasing the neoglucogenesis and glycogenolysis.

These apparently opposite actions of stress on the absorption of certain drugs were interpreted in a recent paper, in which the absorption of various substances was studied in rabbits, following tourniquet trauma[3464]. Based on the finding that under these conditions the absorption of insulin and potassium thiocyanate injected intramuscularly was decreased, while that of substances such as Congo red, dextran or microbial suspension was significantly accelerated, Renaud concluded that dissociation occurs. Certain drugs are absorbed via the blood capillaries and venous circulation, and in this case the rate of absorption is slowed down. On the other hand, the rate at which other drugs are absorbed through the lymphatic system is increased.

Alimentary-tract substances

Finally stress can render the gut permeable for substances present in the alimentary tract but which normally do not traverse it. Compounds such as adrenaline or histamine, which under normal conditions, are only poorly absorbed after oral ingestion, readily enter the blood stream and thus cause intoxication in guinea pigs or rats exposed to cold or musular exercise[3491].

3. *Effect of Stress on the Physiological Action of Drugs*

Vitamins

Following muscular exercise in man, the thiamine tolerance is augmented by about 50%, an indication of the increased need for the vitamin in this condition[3135].

The urinary elimination of ascorbic acid is greatly diminished when this substance is administered to patients after surgical intervention[3160, 3486], accidental injury, extensive burns or spontaneous fractures[3423]. In another report, it was shown that after burns and fractures many patients approach scorbutic levels extremely rapidly, even though the retention of ascorbic acid is tremendously increased and in spite of large daily supplements of the vitamin[3418]. However, not all authors agree unanimously that the retention of ascorbic acid is increased, since it was claimed[3429] that after stress, animals excrete more ascorbic acid in the urine than is given, which indicates a loss of the retaining ability. But it is generally accepted that, in stress, there is a demand for more ascorbic acid and that this demand may come from the adrenal cortex[3423].

Insulin

A few years after the discovery of insulin, it was rapidly recognized that, in man, infections, shock, and surgery increase the need for insulin and sometimes completely inhibit its hypoglycemic action[3459]. It was demonstrated that this condition could be reproduced in rabbits by injecting various infective and toxic agents. After the publication of the stress concept it was established in rats[3467] that this inhibition of the hypoglycemic action of insulin was not due to any specific treatment, but was always present in the alarm reaction elicited by cold, exercise, or formalin injections. More recently, these findings were confirmed by studies in man and in animals. In man, this delay in the insulin response has been described after endocrine, hepatic, or injectious diseases[3446], neoplastic diseases[3426, 3465], and accidental injuries[3488], the most severely injured group showing the least sensitivity to insulin.

In animals, several authors were able to demonstrate a remarkable delay in the hypoglycemic action of insulin in hypothermia[3416, 3470, 3508], after mild exercise[3498] or anesthesia[3496]. Even such stressor agents as sunshine, cold weather, noise, seasons seem to have a definite action on the sensitivity of mice to insulin[3504].

Certain reports seem to contradict this, and state that severe physical exertion can induce a fatal hypoglycemia, following insulin administration [3456, 3498]. Sinse this opposite reaction occurs only in the last stage of exhaustion when the organism is no longer able to mobilize its glycogen reserve because of lack of adaptive hormones[3493], it would not justify basic alterations in our concept of the general effect of stress on insulin treatment.

4. Effect of Stress on the Toxicity of Drugs

Adrenaline and derivatives

Depending on the doses used and on the chronology of the experiments, stress can protect animals against the toxicity of adrenaline, or increase their susceptibility to it. An alarm reaction produced by treatment with formalin, exposure to cold, forced exercise, or surgical trauma increases the rssistance of the rat to the subsequent intravenous injection of lethal doses of adrenaline[3493]. On the other hand, if prior to trauma epinephrine or ephedrine is administered to rats at a dose that in itself has no lethal effect, a high mortality occurs[3461].

Investigations in mice showed that the stress of confinement, produced by crowding the animals together, induced a very high mortality in animals treated with small doses of amphetamine that were not lethal in themselves[3431, 3432, 3443, 3447], the same phenomenon being observed after electric stimulation in rats[3503].

Bacterial toxins

Although it was demonstrated that pretreatment with benzol, total body X-ray irradiation, and nitrogen mustard almost completely suppressed a Schwartzmann reaction induced by two injections of meningococcal toxin[3424], it is usually recognized that the toxicity of one injection of bacterial toxin is potentiated by stress. In this connection, it was demonstrated in guinea pigs that the effect of tetanus toxin was markedly increased by the administration of muscular extracts, the increased toxicity being proportional to the crudeness of the extract[3477]. In experiments with rabbits to which a standard procedure of hemorrhage was applied, it was shown that the rabbits so treated could not safely withstand more than 1/400,000 the dose of a purified *Escherichia coli* endotoxin that normal rabbits can survive[3487]. This basic phenomenon has been confirmed by others in rats[3509] and in rabbits[3417]; it was even concluded that, in toxin treated rabbits, acute stress was as potent in inducing lesions and high mortality as was a preliminary sensitization by the endotoxin itself[3497].

Anesthetics

It is well known that in the presence of an injury in human patients, anesthesia can aggravate an already existing condition of shock, or if shock is impending, anesthesia can precipitate it. Studies on dogs subjected to a controllable and standardized type of hemorrhage presented well-defined differences in the circulatory reaction and collapse between normal or locally anesthetized animals and those completely anesthetized by ether, pentothal or cyclopropane[3427, 3510]. These findings were confirmed in rabbits anesthetized with ether, nitrous oxide or cyclopropane, in which intestinal stripping was applied[3436], and in rats anesthetized with ether after traumatization of the cecum[3502]. It was also reported that thiopental sodium anesthesia was poorly tolerated in patients with large wounds or severe burns[3425].

The depressant action of morphine can be potentiated by trauma, and wounds (particularly with hemorrhage or pneumothorax) and is dangerous in hypothyroidism, obstetrics, and any kind of impaired liver function[3426]. An increase of morphine toxicity under adverse conditions has also been seen in rats and mice placed at different room temperatures[3445].

Finally, in a recent paper[3480] it has been demonstrated that the stress of forced immobilization or of electric stimulation in rats caused a marked increase in the anesthetic activity of sodium bromide.

Antibiotics

Most of the antibiotics when given at high levels may give rise to toxic reactions both in man and animals, which can be even fatal[3439]. Among these reactions, the most frequent is certainly the impairment of the renal function, with a high serum level of non-protein nitrogen that can be conducive to tubular degeneration of kidneys, with cellular and protein casts. These manifestations are seen after administration of a large variety of antibiotics, such as the tetracycline group[3439], streptomycin[3472], polymyxin[3485], bacitracin [3495], neomycin[3505], kanamycin[3507] or even penicillin[3496]. Nevertheless, as a general conclusion there would seem to exist a large variability from one patient to another as regards the dosage of antibiotics that will cause the appearance of toxic manifestations. A possible explanation would be that the toxicity is potentiated by a large number of conditions or agents, such as anesthesia[3434, 3478, 3479], impairment of renal function[3420, 3437, 3454, 3455], neoplastic diseases[3420 3422, 3441], or bacterial toxin administration[3506].

Recently, it was demonstrated in rats that transplanted tumors[3482] could potentiate the toxicity of neomycin sulfate to the point where a very marked nephrocalcinosis, accompanied by large patches of cardiac necrosis, was present in the tumor-bearing rats. The controls had only very minor renal lesions. The same symptoms of neomycin toxicity were finally elicited by a large number of stressor agents, such as forced immobilization, cold baths, quadriplegia, spinal cord transection, intestinal lesions, partial nephrectomy, while almost no lesions occurred in the controls[3487]. These experiments seem to be more significant when one realizes that neomycin is not the only antibiotic to react in this way, the toxicity of kanamycin and bacitracin being potentiated in a similar manner[3483].

Summarizing it can be stated that various stressor agents, such as climatic stress (*e.g.* exposure to cold), muscular exercise, trauma, burns or severe illness, are able to induce marked changes in the absorption and the physiologic or the toxic effects of a large number of drugs. The absorption or the specific drug effect can be either increased or inhibited, depending upon the drug and, sometimes, the chronology of the experiment. In the light of the data reported here, there is no doubt that nonspecific stress and not one condition in particular is responsible for these, sometimes dramatic, toxic effects of pharmacologic therapy seen in such different circumstances.

Section 4. The Influence of Climate on the Geographical Distribution of Disease (Geographical Climatopathology)

by

J. M. MAY

Ever since man began thinking about his fate, observations showing that climate does influence the distribution of human diseases have been made[3511]. But, few analyses of how this relationship is brought about can be found in the literature. In a short chapter, it is not possible to do more than broadly outline general patterns of these relationships and show its complexities. While it is, at our state of knowledge, possible to understand the various channels through which the factors of climate can influence the pattern of disease, it is not wise to deviate from the line of what is strictly proved or extremely likely lest one fall into the kind of folklore that has characterized discussions of problems of climate and disease in the past. Before we start, it is essential that we define what we are talking about.

Of climate we will have little to say as it is described thoroughly in other chapters of this book. To us physicians, and public health workers, climate has to be considered as a composite of many factors, a few of which are understood, most of which are not. This has been revealed recently by the realization of the importance on the human host of such little studied factors as cosmic rays and natural atmospheric radiations. These newly identified forces enter the climatic complex. We are not able in most cases to measure separately the action of the climatic ingredient components, neither can we separate climate's own action on man from that of the living organisms that occur in the various climatic niches.

Disease, however, we should define adequately. Disease to the ecologist is that alteration of living tissues that jeopardizes their survival in a given environment[3514]. This definition stresses survival as the sole purpose of cell function. It also stresses the relative character of disease since cellular alterations may jeopardize survival in one environment while helping it in another: example, polyglobuly, essential to those who live at high altitudes to carry oxygen is probably detrimental at sea level. Under this definition, disease appears as a maladjustment to the environment. Thus, it cannot be separated from the geography surrounding its occurrence. A vast number and types of these maladjustments have been described and are known. For some, we can understand the mechanism that governs their distribution, others only allow us to observe this distribution without understanding its whys and hows. Thus, in order to discuss the influence of climate on the distribution of various types of maladjustment we need to study a little further how these maladjustments occur.

Two sets of factors are necessarily involved: stimuli from the external or internal environment on the one hand, responses from the host on the other; these responses are governed by the genetic makeup of the host. The influence of climate on stimuli and responses is the scope of our assignment. Climate being a composite thing, this section should really consist in discussing the effects that all its components have on the stimuli to maladjustment, and further on the genetic makeup of the host. This of course would be a book in itself.

Students of disease customarily speak of those resulting from the intervention of a living stimulus (bacteria, parasites, etc.) as transmissible, of those resulting from a non-living stimulus as degenerative, and of those allegedly resulting from environmental and emotional stresses as behavioral. This, of course, is quite arbitrary as many living, non-living or situational stimuli often combine in unrecognized proportion to provoke the maladjusted response; for didactic purposes, however, this is a convenient presentation.

Transmissible diseases involve either just an agent and a host (poliomyelitis, cholera, two-factor complexes), or an agent, a vector, and a host (malaria, three-factor complex), or an agent, a reservoir, a vector and a host (plague, four-factor complex); some present themselves as even more complicated complexes such as, for instance, yellow fever whose geographical pattern of distribution can only be explained if one understands the link existing between two separate but connected three-factor complexes: a jungle complex (mosquito, marsupial, virus), and an urban complex (mosquito, man, virus). Epidemics do occur when man goes into the jungle replacing the marsupial in the three-factor complex thus establishing a link between the occurrence of disease in the jungle and its occurrence in the urban area[3516].

Degenerative diseases are also the result of stimuli provoking responses from the host. Examples of diseases that can be classified in this category would be frost-bite, or sunburn, solar ray induced cancers, nutritional and metabolic diseases, etc.

Finally, a third group of diseases is represented by the behavioral disorders where a situation which most individuals would be able to cope with, will result, in a predisposed person, in a behavioral response that is not acceptable to society nor adjusted to environmental reality. Under such circumstances, the survival of this individual in this environment is placed in jeopardy.

How does climate affect these various groups of diseases, the multiple stimuli that cause them in each category, and hence their geographical distribution? Some of the correlations are obvious and do not need to be elaborated. Temperature, humidity, winds will influence the maturation of the malaria parasite in the mosquito, the breeding and longevity of this and other arthropod vectors, the direction of their flight, etc. As a result, epidemics of transmissible diseases occur or not, persist or subside, reappear at every season, or disappear forever.

There are less obvious effects of climate on transmissible diseases and on the elements of the complexes. It must not be forgotten that all living things live in societies. A society is nothing but the temporary expression of a pattern of mutual tolerance that occurs for a very short time only after the forces of reciprocal exclusion have been exhausted. A society of living things is a compromise between struggling individuals for food and shelter; it can be compared to a pyramid at the top of which a few dominants are established tolerating at the lower and broader echelons of the base, subdued individuals whose demands in the environment, in the niche as we ecologists call it, is limited to the crumbs. They have found the ability to survive and to multiply under such conditions of shelter and food availability as the society, such as it is constituted in that niche, at that time, provides for them. As long as no influence from the outside occurs, this society will survive in that niche. Should, however, a new element be introduced in the pyramid, such as for instance, penicillin in the fauna or flora of the intestines, or gambusia fish in a pond where hitherto malaria vectors bred successfully, the social pattern is disturbed, the dominants are destroyed, unknown problems of relationship arise as new living forms come to the top. This is also true if the climate changes; if ponds and rivers dry up, if swamps are filled, if jungle is felled, if new irrigation upsets the area. These new climatic changes benefit new forms of life, cause others to perish. These new social orders among living organisms may or may not be beneficial to man. Thus, man-made malaria occurs as readily as natural malaria can be eradicated.

Any change in temperature, humidity, force of winds arising through natural causes or through man-engineered causes, bring about upheavals in ecological niches. Bacteria, reservoirs, and eventually human hosts all are affected, the social pyramid is upset, and the general pattern of disease distribution is profoundly modified.

In the case of degenerative diseases, we are again confronted with obvious and less obvious influences of climate. Obvious is the influence of such factors as cold and heat in the occurrence of such diseases as frostbites or heat strokes; obvious again is the influence on crops, and hence on nutritional deficiency diseases. Less obvious, however, the role of carcinogenic action of certain solar rays, the effects of strong winds (foehn, sirocco, typhoons) pon the metabolism and the general physiological behavior of the human host. Recent studies tend to discount any measurable influences of these climatic factors. But this may be the result of the crudeness of our measuring instruments. If one remembers that solar flares result in a bombardment of cosmic rays that disrupt electronic communication on earth, one cannot but wonder if these little known aspects of climate cannot also disrupt electronic communications in our cells bringing faulty metabolism and maladjustment as their result.

Climate influences culture, because culture can be considered the sum of concepts and techniques used by man to control his environment. In the delta of the Red River in North Vietman,[3513] where climatic conditions are such that exceptionally rich crops of rice can be harvested three times a year, a considerable number of people have flocked to protect themselves against starvation. But very soon their number has increased to such proportions that they were threatened by precisely what they were seeking to avoid. Their answer to this has been to utilize land to the utmost and reduce residential space to a minimum. Climate has also prevented the establishment in this region of good building timber, with the result that houses are not only very close together but also built with the mud of the rice fields and covered with the straw of the rice. All these factors affect the disease pattern in many ways. From the closeness of the villages and of the houses the people increase their chance of getting tuberculosis. From their thatched roofs they get an abundance of rats and the diseases these rodents carry with them; from the vegetation that grows in the little ponds between the rice field, they get the snails which carry larvae of the lung or the intestinal flukes. Changes in the climate would bring about changes in the social pyramid in which the disease agents, vectors and intermediate hosts are located. Similarly, changes in the architecture, structure, material and many other cultural factors involved in the building of villages would bring about a change in the disease pattern.

Climate also affects the occurrence of mental disorders. Arthropod-borne encephalitides cause certain mental syndromes, and the chain between the influence of climate that allows the breeding of virus-carrying culicines and certain mental diseases, is short. Further, mental disorders and psychoses may either result from or perhaps lead to the absorption of toxic beverages and drug addictions, cultural habits. Climate will influence the choice of a drug: coffee, tea, Indian hemp, coca, or opium, as all of them are available primarily if climate favors the crops from which they are harvested. The psychotic episodes of pellagra are linked to a diet bereft of the pellagra-preventing factors. This diet is again based on crops which are conditioned by a suitable climate. Finally, it can be accepted as a temporary hypothesis that stresses precipitate the occurrence of certain mental and psychic syndromes in predisposed persons (see p. 536). This might explain why schizophrenia seems to be, according to certain statistics, more frequent among populations living in unsatisfactory conditions than among others. This, of course, could not and should not be construed as meaning that crowding is the cause of schizophrenia any more than crowding is the cause of tuberculosis. But we have seen that a cultural factor like the building of a village or the natural growth of a slum area is indirectly the result of the prevailing climatic conditions.

We have thus briefly summarized the many direct or indirect ways through which the physical environment, especially the climate, governs the stimuli that lead to signs of maladjustment in the host.

Let us now discuss the factors that govern the response of the host. These are genetic and more and more importance is now attached to them. A vast field of research concerned with the study of the host and with the exploration of the forces hidden in its chromosomes that make him immune to certain stimuli and sensitive to others is now slowly unfolding. This field seems infinite. Its approaches are hardly chartered as yet. But the role of climate in shaping the genotype of individual hosts or populations is clearly visible. All the mutogenic factors in what we call climate are not known. Various influences such as heat, chemicals and radiations cause mutations to occur at least in plants and forms of life that lend themselves to genetic analysis. Even if they left human genes indifferent, which we have no right to assume, the fact that mutations occur in lower forms of life by necessity will influence the disease pattern of human beings. If it could be proved that the presence of a certain chemical in a body of water can bring about a mutation, changing the virulence of the strain of *Cholera vibrios*, for instance, living in these waters, it would be of great importance in the epidemiology and geographic distribution of cholera epidemics. If floods and rains by changing the chemical composition of bodies of water could determine mutations, the multiplication of water-breeding animals, such as mosquitoes, would undoubtedly affect disease patterns. But without going into speculation we already know that the rate of mutation is governed by the amount of irradiation received at a given spot. All factors that may modify this rate in a given niche will change the disease potential of the population involved, from bacteria to humans. Bacterias in nature will become more virulent or less; vectors' efficiency will be affected; reservoirs will reconsider their relationships with their parasites. Any additional mutogenic factors in the constituents of climates will deeply modify the disease pattern. What the normal geography of mutogenic factors, especially of cosmic radiations was before space travel was considered we do not know, and we know little more about it now, only that they exist and are powerful forces. It is reasonable to assume that these forces did not prevail with the same intensities everywhere above the earth, and that there were niches where the activity of these radiations was greater than in others, thus, governing in living things, dwelling in these parts, a greater number of mutations. The influence of these mutations on disease patterns cannot be doubted, but cannot as yet be scientifically assessed. In a recent publication, Niggli[3515] established that the number of mutations in a given chromosome was depending not only upon the age of the sexual cell studied, but upon a number of factors found in the environment before and after the irradiation. By changing the gaseous contents of the environment, it is possible to lessen eight times the number of mutations. To what degree are the natural forces of climate capable of bringing about such changes, hence modifying or influencing the rate of mutation in living things is not known. But the notion can certainly not be discarded. Turpin and his collaborators have shown that irradiation of 30 r's would produce in man approximately the same amount of mutations as is normally produced in the same lapse of time by natural irradiations. Thus, each time a certain environment receives 30 r's in addition to the normal shower, the number of mutations occurring in man is likely to double. The consequences of this regarding disease patterns are well understood and stressed by Turpin[3517]. These mutations might cause considerable changes in susceptibilities and immunities as well as in the enzymatic system of individuals thus creating a "new host", whose adjustment potential has not yet been tested. The author stresses, rightly it seems to us, that mutations that will not show themselves by some dramatic symptoms such as the absence of a limb, or a crippled brain, will more effectively modify the disease pattern, as they will probably multiply the number of hosts susceptible to as yet unknown new pathogens. Here again the influence of climate on the host through its action on mutations is a new aspect of the role climate plays in affecting the distribution of disease patterns. It is by no means the only one.

Climate governs the "livability" of environment affecting all forms of life in the niche from the unicellular up to the human. Changes in climatic conditions directly and indirectly affect migrations of populations, animal and human. While the migrations of lower animals from one area to the other have not been recorded, human migrations have. A large number of them have occurred as the result of the pressure brought to bear on human communities by changes in climate which have gradually made the environment unlivable. On the contrary, people have been attracted to certain places whose climatic appeal and fertility was a lure that could not be resisted. Floods and droughts have also chased away many populations and so have cultural and political pressures. The results of these migrations, those of lower animals, as well as those of human beings, have always resulted in unrecorded and unanalyzed pooling and segregation of new genes to the places where the newcomers arrive. Whether as conquerors or as peaceful immigrants, there is no doubt that in the long run considerable admixture of new genes has resulted in new population genotypes, with new diseases and new maladjustment properties.

Conclusions

From the life of single protozoa to the life of a large human community, climate governs the patterns of maladjustment (or diseases) that occur among them. It does so by its action on the habitability of the niche, through its food and shelter resources, through its action on biotics and through its influence on the cultural life.[3512] Table 41 is an analytical study of the action of certain factors of climate on certain pathogens in selected transmissible disease complexes. While reading the table it must not be forgotten that a high degree of interrelationship occurs between geogens as well as between pathogens. As it is, the table is given as a thought provoking tool where gaps of knowledge are clearly indicated, rather than as a final statement of facts. Thus, all stimuli to maladjustments can directly or indirectly be traced back to climate. Eventually, the host himself, his genetic makeup, is dependent upon mutations that occur under the direct or indirect influence of the physical environment created by the climate. These concepts although in some ways very obvious are not part of the pattern of thinking of physicians, which is why we thought they were worth introducing in this book.

Section 5. Climatotherapy

Subsect. A. PRINCIPLES INVOLVED IN AEROSOL AND IONIC TREATMENT

1. *Aerosol Treatment*

General principles

On p. 102 Bisa reviewed the physical properties of aerosols, consisting of naturally or artificially dispersed solid or fluid particles in the atmosphere, the size of which may fluctuate between 2 mμ and 5μ. It was pointed out on p. 104 that the relatively small mass of aerosol particles, as compared with their surface, is mainly responsible for their greater physico-chemical activity. With decreasing size of the particles their total surface increases; therefore the speed of various chemical reactions with the environment is accelerated.

The mechanism of the penetration of solid particles into lungs was described on p. 301. It is the particles smaller than 3μ, in particular, which can reach the alveoli. The smaller the particles and the higher the electric charges of these particles, the greater their velocity and depth of penetration. Up to 90% of an aerosol with particles of 0.1 μ, each with a great electrical charge, will remain in the lungs, where the particles are precipitated. Aerosol treatment of this kind, carried out in a climatic chamber of low atmospheric pressure, increases considerably the interaction between the aerosols and the cells of the pulmonary alveoli by increasing the pulmonary ventilation (see p. 293). The principal purpose of aerosol treatments is the following: (*i*) Direct intensified physico-chemical treatment of diseased parts of the respiratory passages. (*ii*) Indirect treatment of other organs by inhalation of certain drugs which are absorbed in the lungs and may reach various diseased parts of the body.

Methods used

Four methods, different in principle, are generally used in aerosol treatment which are fully described on pp. 633–635 by Nückel and Lincke. The patient is placed in so-called aerosol chambers for the aerosol treatment.

(1) In the *acid-spray chambers*, acid aerosols or acid vapours are used, these being created by an artificial air current which evaporates and spreads certain acid solutions stored on open plates. The method was introduced in Germany by Kapff, who observed many years ago that respiratory infections seem to occur less among factory workers, who work in an atmosphere of acid vapours or aerosols.

(2) In the *ultrasonic-spray chambers* the pharmaceutical products are sprayed as fine aerosols by means of ultrasonic waves.

(3) *Salt water-spray chambers* use aerosols; these are not for direct treatment of the respiratory passage, but the lungs act as an intermediary organ required for the absorption of certain drugs required for the treatment of other organs of the body.

A variety of drugs have been used for aerosol treatment in these chambers. They are fully described by Friebel in Nückel's textbook *Aerosol Therapie* (F-K. Schattauer Verlag, Stuttgart, 1957, pp. 85–119). The pharmaceutical products, used in aerosol treatment, can be classified into the following four groups:

TABLE 41 (Courtesy of the *Icographical Review*)

	Altitude	*Latitude*	*Luminosity*	*Nebulosity*	*Water drainage*	*Rainfall & humidity*	*Barometric pressure*	*Temperature*	*Winds*	*Radiation*	*Magnetism*	*Static electricity*	*Ionization*	*Vegetation*	*Soil conditions*	*Income*	*Population density*	*Housing*	*Sanitation*	*Clothing*	*Diet*
Two-factor complexes																					
Epidemic	—	—	—	—	?	?	?	?	?	?	?	?	?	—	—	—	+	—	+	—	?
meningitis	—	—	?	?	?	?	?	+	?	?	?	?	?	?	?	—	—	—	+	—	?
Epidemic	—	—	—	—	+	+	?	?	?	?	?	?	?	?	?	+	+	+	+	—	+
cholera	—	—	—	—	+	+	?	+	?	?	?	?	?	?	?	—	+	+	+	—	?
Endemic	?	?	?	?	?	+	?	?	?	?	?	?	?	?	?	+	?	+	+	—	+
cholera	?	+	?	?	+	+	?	+	?	?	?	?	?	?	?	—	+	—	+	—	?
Bacillary	—	—	—	—	+	+	?	?	—	?	?	?	?	?	?	+	+	+	+	—	+
dysentery	—		+	+	+	+	?	+	?	?	?	?	?	?	?	—	+	+	+	—	?
Typhoid fever	—	—	—	—	+	+	?	?	—	?	?	?	?	—	—	+	+	+	+	—	+
group	—	—	+	+	+	+	?	+	?	?	?	?	?	?	?	—	+	+	+	—	?
Tuberculosis	+	—	+	+	+	+	+	+	+	?	?	?	?	+	?	+	+	+	+	—	+
	+	—	+	+	+	+	?	+	?	?	?	?	?	—	?	—	+	+	+	—	+
Diphtheria	—	?	?	?	?	?	?	?	?	?	?	?	?	—	—	—	+	+	+	—	—
	?	?	?	?	?	?	?	+	?	?	?	?	?	?	?	—	+	+	+	—	—
Scarlet fever	—	+	?	?	?	?	?	?	?	?	?	?	?			—	+	+	+	—	—
	—	?	?	?	?	?	?	+	?	?	?	?	?	—	—	—	+	+	+	—	—
Brucellosis	—	—	—	—	+	?	?	?	—	?	?	?	?	—	—	+	—	—	+	—	+
	—	—	+	+	+	+	?	+	?	+	?	?	?	?	?	—	—	—	+	—	+
Gonorrhea	—	—	—	—	—	—	—		—	—	—	—	—	—		—	—	—	+	—	—
	—	—	—	—	—	—	—	+	—	—	—	—	—	—	—	—	—	—	+	—	—
Anthrax	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	+	—	—
	?	?	?	?	?	?	?	+	?	?	?	?	?	?	?	—	—	—	+	—	—
Leprosy	—	—	—	—	—	—	?	?	?	?	?	?	?	—	—	—	+	—	+	—	?
	—	—	?	?	?	?	?	+	?	?	?	?	?	—	—	—	—	—	+	—	—
Tetanus	—	—	—	—	—	—	—	—	—	?	?	—	—	—	—	—	—	—	+	—	—
	?	?	?	?	?	?	?	+	?	?	?	?	?	?	+	—	—	—	+	—	—
Poliomyelitis	—	—	?	?	?	?	?	+	?	?	?	?	?	?	?	—	+	—	—	—	?
	?	?	?	?	?	?	?	+	?	?	?	?	?	?	?	—	?	—	—	—	?
Influenza	—	—	?	?	?	+	?	+	?	?	?	?	?	—	—	—	+	+	+	+	+
	?	?	?	?	?	+	?	+	?	+	?	?	?	?	?	—	+	+	+	—	?
Measles	—	—	?	?	?	?	?	?	?	?	?	?	?	?	—	—	+	+	+	—	—
		—	?	?	?	?	?	+	?	?	?	?	?	?	?	—	+	+	+	—	—
Smallpox	—	—	?	?	?	?	?	?	?	?	?	?	?	—	—	—	+	+	+	—	—
	—		?	?	?	?	?	+	?	?	?	?	?	?	?	—	+	+	+	—	—
Lymphogranu-	—		—	—	—	—	—	—	—	?	—	—	—	—	—	—	—	—	+	—	?
loma venereum	—	—	—	—	—	—	—	+	—	+	—	—	—	—	—	—	—	—	+	—	—
Amoebic	—	—	—	—	+	+	—	—	—	—	—	—	—	?	?	—	—	+	+	—	+
dysentery	—	—	—	—	+	+	—	+	—	—	—	?	?	?	?	—	—	+	+	—	+
Ascariasis	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	+	+	+	+	—	+
	+	+	+	+	+	+	?	+	?	+	?	?	?	+	+	—	+	+	+	—	—
Ancylostomiasis	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	+	+	+	+	+	+
	+	+	+	+	+	+	?	+	?	+	?	?	?	+	+	—	+	+	+	+	—
Syphilis	—	+	?	?	—	—	—	—	—	—	—	—	—	—	—	—	—	—	+	—	—
	?	+	?	?	?	?	?	+	?	?	?	?	?	—	—	—	—	—	+	—	—
Yaws	+	+	?	?	—	+	—	?	—	—	—	—	?	?	—	+	+	+	+	+	?
	+	+	?	?	?	+	?	+	?	?	?	?	?	?	?	+	—	—	+	+	?
Pinta	?	+	?	?	—	—	—	?	—		—	—	?	?	—	+	+	+	+	+	?
	?	+	?	?	?	+	?	+	?	?	?	?	?	?	?	+	—	—	+	+	?

* It has seemed preferable, in working out this table, to consider man only in relation to other factors and not as an different agents of the complex. For example, housing affects man with

ROVISIONAL CORRELATIONS BETWEEN GEOGENS AND PATHOGENS*

Drug addictions	*Communications*	*Animal life*	*Parasitism*	*Relation to other diseases*	*Partial pathological complexes*	*Dominant blood groups*	*Remarks*	*Pathogens*
? —	· -	— =	? ?	? ?	—	? ?	Rainfall, humidity, and water drainage may influence infection by droplets	Man *Meningococcus*
?	·	— ?	 ?	? ?	? ?	? ?		Man *V. cholerae*
?	· —	? ?	? ?	? ?	? ?	? ?	The nidification of the disease is governed by unknown factors	Man *V. cholerae*
?	·	— ?	? ?	? ?	—	? ?	Flies may play a part in the spread of the disease, but their role is mechanical rather than biological	Man *Shigella* & *group*
? -	+	— ?	? ?	? ?	—	? ?	Flies may play a part in the spread of the disease, but their role is mechanical rather than biological	Man *Eberthella* & *group*
+ —	-- —	+ +	-	? ?		? ?	Infected droplets play a part in the spread of the disease	Man *M. tuberculosis*
· —	+ —	 —	 —	 —	 —	? ?	Infected droplets play a part in the spread of the disease	Man *C. diphtheriae*
 —	 —	 ·	 —	? ?	 —	? ?		Man *S. scarlatinae*
 —	+ —	+ +		+ +	+ ·	? ?		Man *B. melitensis* & *group*
 —	 —	—	 --		 --	? ?		Man *N. gonorrhoea*
+	—	+	—	—	—	? ?	The spores of *B. anthracis* remain viable in soil indefinitely. Geographical factors influencing the soil may influence the spores	Man *B. anthracis*
? —		 ?	 —	 ?	 —	? ?		Man *M. leprae*
—	—	+ ·	—	+	+ +	? ?	*C. tetani* is widely distributed in the soil and therefore probably sensitive to geographical factors influencing the soil	Man *C. tetani*
? ?		? ?	? ?	? ?	? ?	? ?	Epidemiology still under discussion; infected droplets may play a part in the spread of the disease	Man Viruses
? —	 +	? ?	? ?	? ?	? ?	? ?	Epidemiology still under discussion; the respective roles of the different viruses, the role of animal reservoir, and the passage from endemicity to epidemicity are not clear. Droplet infection is certain	Man Viruses
?	+ ·	-- ?	? ?	? ?	? ?	? ?	Air-borne infection by droplets is probable means of spread	Man Virus
? —	· ·	-- ?	--	· +		? ?	Air-borne infection by droplets probable. Correlation has been found between incidence of smallpox and aqueous vapor tension in India and England	Man Viruses
—	—	-- -	--	--	--	? ?	The virus is destroyed by ultraviolet rays	Man Viruses
-	+		? ?		+ +	? ?	Seasonal variation of incidence has been observed. Humidity seems more important than temperature	Man *E. dysenteriae*
	· ·	· +	+ +		+ +	? ?	Warmth, moisture, and oxygen influence the development of the embryo outside the body. Ova are resistant to cold and dryness	Man *A. lumbricoides*
 —		· +	+ +		+ ·	? ?	Porous, sandy soil and shade favor the growth of the larva	Man *A. duodenale* & *group*
	 -					? ?	Man does not seem to respond in the same way to *T. pallidum* in different latitudes	Man *T. pallidum*
?	—	—	—	? ·	—	? ?	Disease limited to low humid tropics. At high altitudes, lesions dry up. The role of flies in transmission is mechanical	Man *T. pertenue*
?	--			? +		? ?	Prevalent in warm humid tropics, especially along stream banks; *Simulium haematopotum* may help spread mechanically	Man *T. carateum*

ated element, since his response to the various geogens may make him more or less receptive to the actions of the
rd to malaria but not with regard to clonorchiasis or syphilis.

TABLE 4

	Altitude	*Latitude*	*Luminosity*	*Nebulosity*	*Water drainage*	*Rainfall & humidity*	*Barometric pressure*	*Temperature*	*Winds*	*Radiation*	*Magnetism*	*Static electricity*	*Ionization*	*Vegetation*	*Soil conditions*	*Income*	*Population density*	*Housing*	*Sanitation*	*Clothing*	*Diet*
Three-factor complexes																					
	—	—	—	—	—	—	?	?	?	?	?	?	?	?	—	—	+	—	—	+	?
Dengue	+	+	+	+	+	+	+	+	+	+	?	?	?	+	+	—	+	+	+	+	+
	?	?	—	?	?	—	?	+	?	—	?	?	?	?	—	—	—	—	—	—	—
	+	—	?	?	—	—	?	+	?	?	?	?	?	—	—	+	—	+	+	+	+
Malaria	+	+	+	+	+	+	+	+	+	+	?	?	?	+	+	—	+	+	+	+	+
	?	—	?	?	?	?	?	+	?	?	?	?	?	?	?	—	+	—	+	—	—
	—	+	—	—	—	—	?	?	?	?	?	?	?	?	—	+	+	+	+	+	?
Trypanosomiasis	+	+	+	+	+	+	+	+	+	?	?	?	?	+	+	—	—	+	+	—	+
	—	+	?	?	?	?	?	+	?	?	?	?	?	+	?	—	—	—	+	—	—
Filariasis	—	—	—	—	—	—	?	?	?	?	?	?	?	—	—	+	+	+	+	+	?
Type:	+	+	+	+	+	+	+	+	+	+	?	?	?	+	+	—	+	+	+	+	+
W. bancrofti	+	+	?	?	—	+	?	+	—	?	?	?	?	—	—	—	—	—	—	—	—
Filariasis	—	—	—	—	—	—	?	?	?	?	?	?	?	—	—	+	+	—	+	—	+
Type:	?	?	?	?	+	+	?	?	?	?	?	?	?	?	?	—	—	—	+	—	—
D. medinensis	?	+	?	?	—	?	?	+	—	?	?	?	?	?	?	—	—	—	+	—	—
	—	—	—	—	—	—	?	?	?	?	?	?	?	+	?	+	+	—	+	+	?
Schistosomiasis	—	+	?	?	+	+	?	+	?	?	?	?	?	+	+	—	—	—	—	+	—
	—	+	?	?	+	+	?	+	?	?	?	?	?	+	+	—	+	—	+	+	?
Cestode diseases	—	—	?	?	?	?	?	?	?	?	?	?	?	?	?	—	—	—	—	—	—
Type:	—	—	?	?	?	?	?	?	?	?	?	?	?	?	?	—	—	—	+	—	—
T. echinococcus	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	—	—	—	+	—	—
Relapsing	+	+	+	+	?	?	+	+	?	?	?	?	?	—	—	+	+	+	+	+	+
fevers	+	+	?	?	?	+	+	+	—	?	?	?	?	—	—	—	+	+	+	+	—
	—	—	?	?	?	?	?	+	—	?	?	?	?	—	—	—	+	—	—	—	—
Leptospiral	—	—	?	?	+	—	?	?	?	?	?	?	?	?	?	—	—	+	+	—	—
diseases	—	—	?	?	—	—	?	?	?	?	?	?	?	?	?	—	—	—	+	—	+
	—	—	?	?	+	+	?	+	?	?	?	?	?	?	?	—	—	—	—	—	—
Epidemic	—	—	+	+	—	—	+	+	+	?	?	?	?	?	?	+	+	+	+	+	+
typhus	—	—	—	—	—	—	?	?	?	?	?	?	?	?	?	—	—	—	+	+	?
	—	—	?	?	—	—	?	+	?	?	?	?	?	?	?	—	—	—	+	—	+
Four-factor complexes																					
	—	—	—	—	—	—	?	?	?	?	?	?	?	?	?	—	+	—	+	+	?
Scrub	—	—	—	—	—	—	?	?	?	?	?	?	?	?	?	—	+	+	+	—	—
typhus	?	+	?	?	+	+	?	+	?	?	?	?	?	+	+	—	—	—	—	+	—
	—	—	?	?	—	—	—	+	—	?	?	?	?	—	—	—	—	—	+	—	?
	—	—	—	—	—	—	?	?	?	?	?	?	?	+	—	—	—	—	+	—	—
Tularemia	—	—	?	?	?	?	?	+	?	?	?	?	?	+	—	—	—	—	+	—	?
	—	—	—	—	—	—	?	?	?	?	?	?	?	—	—	—	—	—	+	?	?
	—	—	?	?	—	—	?	+	?	?	?	?	?	—	—	—	—	—	+	—	?
Trematode	—	+	?	?	—	?	?	?	?	?	?	?	?	—	—	—	—	—	+	—	+
diseases	—	+	?	?	+	+	?	?	—	?	?	?	?	+	+	—	—	—	—	—	—
Type:	—	—	?	?	+	+	?	+	—	?	?	?	?	+	+	—	—	—	+	—	—
Clonorchiasis	—	—	?	?	+	+	?	+	—	?	?	?	?	+	+	—	—	—	+	—	—
	—	—	?	?	—	?	?	?	?	?	?	?	?	—	—	—	—	—	+	—	+
Cestode	?	?	?	?	+	+	?	?	?	?	?	?	?	?	?	—	—	—	+	—	—
diseases	—	—	?	?	+	+	?	?	?	?	?	?	?	?	?	—	—	—	+	—	—
Type: *D. latum*	—	—	?	?	+	+	?	?	?	?	?	?	?	?	?	—	—	—	+	—	+
	—	—	?	?	—	—	?	—	?	?	?	?	?	?	?	—	—	+	+	—	—
Bubonic plague	?	—	?	?	?	+	?	+	+	?	?	?	?	—	?		—	—	+	+	?
	?	?	?	?	?	?	?	+	?	?	?	?	?	—	?	+	+	+	+	+	?
	—	—	?	?	?	?	?	+	?	+	?	?	?	—	?	—	—	—	+	—	—
	—	—	—	—	—	—	?	?	?	?	?	?	?	—	—	+	+	—	+	+	—
Yellow fever	+	+	+	+	+	+	+	+	+	+	?	?	?	+	+	—	+	+	+	+	+
	?	+	?	?	?	?	?	+	?	?	?	?	?	+	+	—	—	—	—	—	?
	—	+	?	?	?	?	?	+	?	?	?	?	?	+	?	—	—	—	—	+	—
	+	+	?	?	+	+	?	+	?	?	?	?	?	?	—	+	+	+	+	+	?
Leishmaniasis	+	+	+	+	+	+	+	+	+	+	?	?	?	+	+	—	+	+	+	+	+
	+	+	?	?	?	+	?	+	?	?	?	?	?	?	?	—	—	—	—	—	?
	+	+	?	?	+	+	?	?	?	?	?	?	?	?	?	—	+	—	+	—	?

(continued)

Religious customs	*Drug addictions*	*Communications*	*Animal life*	*Parasitism*	*Relation to other diseases*	*Partial pathological complexes*	*Dominant blood groups*	*Remarks*	*Pathogens*
—	—	—	—	—	—	—	?	*Aëdes aegypti* has been seen up to 5000 ft. but is limited to 40° N.–40° S. latitude	Man Mosquito Virus
—	?	+	+	+	—	+	?		
—	—	—	—	—	+	—	?		
—	+	+	—	—	?	+	?		Man Anopheles *Plasmodium*
—	?	+	+	+	?	+	?		
—	+		+	?	?	+	?		
—	?	+	+	—	+	+	?	In some regions wild game and the native pig act as reservoirs. High temperatures favor the development of the parasite in flies	Man Fly or bug *Trypanosoma*
—	?	—	+	+	+	+	?		
—	—	—	+	—	+	+	?		
—	?	—	—	+	+	—	?	Antelope and buffalo may act as reservoirs for *Onchocerca* in Africa	Man Fly, mosquito, or tabanid *Onchocerca, Wuchereria, Loa*
—	?	+	+	+	+	—	?		
—	—	—	—	+	+	—	?		
+	?	—	—	—	+	—	?		Man Copepod *Dracunculus*
—	—	—	+	+	+	—	—		
—	—	—	+	+	+	—	?		
—	?	—	+	+	+	+	?		Man Snail *Schistosoma*
—	—	—	+	+	+	+	—		
—	—	—	+	+	+	+	?		
—	—	—	+	+	—	—	?	In this complex man is an accidental factor and a dead end for the parasite	Dog Sheep- Man *E. granulosus*
—	—	—	+	+		+	?		
—	—	—	+	+	?	+	?		
—	?	+	+	+	?	+	?	Malnutrition seems to be a predisposing factor in man. Cold weather favors lousiness. Vector may be transported over long distances. Infection is transmitted to next generation. In California a fourth factor may enter in, since some rodents are a reservoir for spirochetes	Man *Pediculus or Ornithodoros* Spirochete
—	—	+	+	+	?	+	?		
—	—	+	+	+	?	+	?		
—	—	—	+	+	—	+	—	Seasonal correlations have been recorded in various parts of the world. Correlation has been shown between survival of spirochetes and salinity of water in which they live	Rodent Man *Leptospira*
—	?	—	+	+	—	+	?		
—	—	—	—	+	—	+	?		
—	?	+	—	+	+	—	?	Cold weather favors lousiness	Man Pediculus *R. prowazeki*
—	?	—	+	+	—	—	?		
—	?	—	—	+	+	—	?		
—	?	?	+	+	+	+	?	The adult mite lives on a certain type of grass, such as the coarse grasses growing on abandoned estates	Man Rodent Larval mite Rickettsia
—	—	?	+	+	+	+	—		
—	—	+	+	+	+	+	?		
—	?		?	+	+	+	?		
—	—	—	+	+	—	+	—	*Dermacentor* is vector and also reservoir, since it remains infected all its life; transmits infection to its eggs. The disease may be transmitted directly	Rodent *Dermacentor, Ixodes* Man *P. tularensis*
—	?	—	+	+	—	+	?		
—	?	—	+	+	+	+	?		
—	?	—	+	+	+	+	?		
—	—	—	+	+	—	+	?	Some trematodes do not require a second intermediate host. The cercariae erupt and attach themselves to certain types of aquatic vegetation	Man Snail Fish Fluke
—	—	—	+	+		+	—		
—	—	—	+	+	—	+	—		
—	—	—	+	+	—	+	?		
—	—	—	+	+	—	+	?	The spargana of similar parasites cannot be distinguished	Man Copepod Fish *D. latum*
—	—	—	+	+	+	+	—		
—	—	—	+	+	+	+	—		
—	—	—	+	+		+	—		
—	+	+	+	+	—	+	—	Only bubonic is considered here, since pneumonic plague is usually transmitted from man to man	Rodent Flea Man *P. pestis*
—	—	—	+	+	—	+	?		
—	?	+		+	—	+	?		
—	—	—	—	+	—	+	?		
—	?	+	+	?	?	+	?	Yellow fever seems to be maintained by a dual cycle: jungle yellow fever where the virus is maintained in the primate by a mosquito (*Haemagogus*) and household yellow fever spread by the cycle man-mosquito (*Aedes*)	Man Mosquito Jungle reservoirs Virus
—	?	—	—	—	—	+	?		
—	—		+	+	?	+	?		
—	?		+	—	?	+	?		
—	?	—	+	+	+	+	?	Debatable whether the various leishmaniases should be considered a three- or four-factor complex. In China the dog seems to be an important reservoir	Man *Phlebotomus* *Leishmania* Reservoir (Dog)
—	?	—	+	+	+	+	?		
—	—	—	+	?	+	+	?		
—	—	—	+	—	+	+	?		

(1) *Antibiotics and chemotherapeutics.* Antibiotics comprise a group of chemical compounds, usually produced by and obtained from lower plant cells (bacteria, moulds, etc.), with a destructive action on pathogenic or noxious organisms. Similar, artificially synthesized compounds are known as chemotherapeutics. For aerosol treatment substances like penicillin, streptomycin, aureomycin, certain sulphonamides, etc. have been recommended.

(2) *Spasmolytics* comprise various chemical compounds used against bronchospasms either directly (through the bronchial muscles) or indirectly (through the autonomic nervous system). Examples are adrenaline, aludrine, ephedrine, anticholinergics (*e.g.* atropin), ethyl papaverin and khelline (directly affecting the bronchial muscles) and so forth.

(3) *Anti-inflammation substances* comprise various chemical compounds which either destroy or absorb locally irritating substances in the respiratory tract. Absorbents in particular are often used in aerosols, *e.g.*, aetherial oils and balsams (such as camomile, fir-needle, eucalyptol and turpentine oils.)

(4) *Secretolytics* comprise substances which promote the secretion and fluidity of substances collected in the lower parts of the respiratory tract. Examples of expectorants (*i.e.* substances promoting ejection of sputum from the air passages) are various aetherial oils, saponins, creosote, etc.

Clinical applications

Vasomotor *rhinitis* (see p. 462) is often successfully treated with a slightly heated inhalation spray of aerosol particles of 10–50 μ. Different aetherial oils have been recommended.

Sinusitis (inflammation especially of the maxillary sinus of the nose) is usually little affected by aerosols consisting of large particles. According to Nückel however, aerosols of antibiotics of 0.5–5 μ may have good results.

Chronic laryngitis (inflammation of the larynx) is sometimes successfully treated with fine aerosols of $^1/_4$–$^1/_2$% hypotonic salt solutions, causing a swellling of the tissue cells (contrary to hypertonic solutions, which cause a shrinkage of cells)*. Usually also aetherial oils are added to the aerosol.

Bronchial asthma is often successfully treated with various spasmolytic aerosols, especially in combination with low-pressure chambers.

Whooping cough (see p. 533) can be succesfully treated, according to Imperato, by using aerosols containing 75–100 mg streptomycin for a

* An iso-osmotic pressure of tissue fluids requires a 0.9% NaCl, 1.8% Na_2SO_4 and 3.4% $MgSO_4$ solution. Therefore each thermal water requires different concentrations if an isotonic solution is required.

period of 8–14 days. Similar good results are obtained with chloramphenicol in 10% propylenglycol.

The best results may be obtained if these aerosol treatments are carried out in low-pressure climatic chambers (see p. 638).

Further examples of aerosol treatment are discussed by Nückel on pp. 633–635.

2. *The Clinical Effects of Aero-Ionization*

by

I. H. KORNBLUEH and F. P. SPEICHER

From the beginning of this century electric space charges or ions have influenced the thinking of a generation of scientists. As early as 1902, Aschkinass and Caspari[3659], independently from Sokoloff[3664], assumed that ionized air is of biological significance. In the following three decades scores of scientific papers were devoted to this topic. From the great number of investigators who until the late 1930's have eminently influenced the development of artificial ionization, a few should be mentioned here: Tchijevsky[3663], Dessauer [3643], Edström[3644], Yaglou[3668] and Bierman[3636] and their collaborators. After 1933, political developments in Europe disrupted for a long time this field of research and for many years only the Russian school headed at that time by Tchijevsky continued this work. The Second World War silenced even this last source of information.

Interest in artificial ionization was revived after the war. Improved generators and ion counters permitted a broader approach and in a very few years research teams in the United States and the Soviet Union added substantially to our meager knowledge of the physical, technical, physiological and clinical aspects of artificially ionized air (see pp. 351–369).

The therapeutic potentialities of unipolarly ionized air were studied long before its physiological action was clearly understood. The results are most encouraging, if admittedly not entirely uniform. Lack of established rules in the clinical work and complete disregard of environmental factors are partly responsible for the occasional failures and thus, indirectly, for the somewhat dragging popularization of this therapeutic method.

Observations made on hundreds of persons of different races, colors, age groups and sex have shown that a relatively high percentage of people do not respond, either subjectively or objectively, when exposed to unipolar electric space charges[3625]. This individual equilibrium or selectivity suggests, if only empirically, the existence of a constitutional factor. Also, it should be mentioned that young persons in good health show a remarkably fast adaptation to a changing milieu of ions and, therefore, are least suitable for clinical experimentation.

Two methods of ion generation are presently being used in the United States: radioactive emitters of the Wesix type and electrostatic generators made expressly for experimental purposes by the Philco Corporation. In the Soviet Union three types of ionizers were developed: the electro-effluvial designed by Reynet and Pruller, the hydrodynamic of the Chernyavsky – Pyslegin type and a radioactive generator constructed by Verigo and Steinbeck. The last two methods of ion generation are most commonly used. Undesirable gaseous by-products are well controlled in both countries. In Germany and Sweden hydro-ionization enjoys some popularity.

In recent years impressive clinical and experimental work was reported from Germany, the United States, the USSR, Czechoslovakia and Rumania, which contributed much to our understanding of the physiological action of aero-ions. The late Salvator Cupcea and his co-workers of the Institute of Hygiene of the Medical School in Cluj, Rumania[3638, 3639], studied the rate of survival of epinephrectomized rats and guinea pigs in artificially induced anaphylactic shock. The animals exposed to negatively ionized air showed a higher rate of survival as compared to controls and those exposed to positive ionization. Vasiliev[3665, 3666], summarizing the findings of Skorobogatova, Kunevitch, Bratschikova and others, stated that, contrary to other physiotherapeutic agents, air ions enter the body by the way of the respiratory tract. Their action seems to be two-fold: (*i*) Reflectory, by stimulation of the pulmonary interoceptors and (*ii*) Humoral, through the blood. The findings of Krueger and Smith[3655], reported on pp. 353–362, suggest most convincingly also a direct action of ionized air on exposed and isolated animal tissues.

While the effects of positively ionized air were subjected to thorough tests by Schorer[3660], Cupcea[3638, 3639], Frey[3645], Zwonisky and Obrossov[3656] and Winsor and Beckett[3667], showing frequently most significant results, in medicine only ions of the negative polarity are currently employed. It seems, however, that certain conditions respond better to positively ionized air and are unaffected or occasionally adversely affected by the negative polarity. This observation was made on patients with coronary artery disease but the number of cases is insufficient for statistical evaluation. Minkh[3658] thinks that the advisability of treatment with positive air ions should not be entirely dismissed. He underscores the possibility that identically charged ions may produce different effects in different concentrations and under different experimental conditions, as "the effect of identical doses may vary depending on the length of exposure and that heavy doses administered in a few seances may act differently than small ones given over a longer period of time". In the opinion of Minkh, as quoted by Malysheva-Kraskevich[3656], it is conceivable that in certain combinations with definite experimental conditions, including the individual characteristics of the patient and his general condition, oppositely charged ions will not always produce a reverse biological effect.

Malysheva-Kraskevich[3656] states that the beneficial action depends largely on the density of negative air ions as a very small dose produces no noticeable effects while an excessive dose might be harmful. A careful review of the literature fails to reveal any toxic effects even after repeated long seances in artificially ionized rooms. However, it should be mentioned that continuous exposure to high levels of ionized air is not desirable and that the great majority of clinical investigators prefer intermittent, short exposures. Despite the many basic differences in the technique there is a substantial agreement on the effectiveness of aero-ions.

Definite therapeutic results were reported in cases of bronchial asthma, sinusitis and hay fever by Bierman[3636], Kornblueh, Speicher, Griffin and Piersol[3648-3654]. Over a period of five years nearly four hundred persons allergic to ragweed and other late summer grass pollens with symptoms of conjunctivitis, nasal and pharyngeal irritation, lacrimation, sneezing and other signs of hay fever were subjected to positive and negative ionization with adequate controls. Partial to complete cessation of all symptoms was noted in excess of 60% of all treated persons. Even an artificially induced increase in the number of pollens as compared with the outdoors has not changed the uniformly satisfying results achieved with negatively ionized air. Exposure to positive aeroionization has never brought any relief and in many instances has aggravated the pre-existing condition. Similar observations were made on patients with bronchial asthma caused by air borne allergens. The improvement obtained in this group of patients frequently lasted for many hours while patients with hay fever were comfortable only for relatively short periods of time after leaving the clinic. Initially, patients were seated in artificially ionized rooms for various lengths of time, usually not exceeding one hour. In the following years, the exposure was limited to 30 minutes. This did not affect the quality and degree of relief. The applied air ion concentration varied depending on the distance of the patient from the generator, averaging about 3,000 to 7,000 ions/cm^3 of air.

Dryness of the mucous membranes of the upper respiratory tract and mouth, relaxation and sleepiness were observed by Silverman *et al.*[3661]. This was true of either polarity, slightly more frequently with negative than positive. The electro-encephalographic studies[3662] conducted by Silverman and his co-workers revealed a drop in the alpha frequency between 0.5 and 1.5 c/s during exposure to positive or negative ionization while the control EEG's remained normal in all subjects except one who had a borderline record.

The relaxing, soporific, deodorizing and desiccating quality of negatively ionized air induced David, Minehart *et al.*[3641, 3642, 3657], to introduce this method in traumatic surgery. Persons with various kinds and degrees of burns were treated upon admission to the hospital for 25–30 minutes with negative aero-ions. This was repeated two to three times daily on all in-patients while ambulatory patients received this therapy only once a day. An immediate relief from pain and a gradual drying up of the denuded surfaces followed by scab formation was observed on the majority of over 150 patients with thermal and chemical burns. Independently from these series of treatments, David and Minehart[3640] used, under strictly controlled conditions, during a period of one year, negatively ionized air on nearly 230 post-operative cases. An analgesic effect was noted in a relatively low but significant percentage of these patients.

Somewhat controversial are the statements on the blood pressure lowering effects of repeated exposures of patients with elevated systolic and diastolic pressure. The results lacked uniformity and could not be duplicated by other investigators.

Work with artificially ionized air enjoys a high priority in the Soviet Union. Sponsored by the Pavlov Institute of Physiology of the Academy of Sciences of the USSR in Leningrad, and under the direction of Vasiliev[3664], numerous hospitals and health centers have adopted this method as routine therapy. Bulatov of Leningrad[3650], Chernyavsky of Tashkent, Minkh of Moscow[3658] and many others are actively engaged in this work. Adequate research and professional staffs are available. Negatively ionized air is being recommended by the Russian school for the following conditions: essential hypertension, ozena (*i.e.* atrophic rhinitis with an offensive nasal discharge), bronchial asthma, delayed healing of wounds, aphtous stomatitis (*i.e.* inflammation of the oral mucosa), neurodermatitis and the after effects of some forms of arthritis and allied conditions.

Overwhelming evidence favors application of ionized air in medicine. However, much work remains to be done. Standardization of ion generators and counters, establishment of reliable doses and means of determination of individual tolerance must be accomplished first before aeroionization becomes acceptable as an adjunctive form of therapy in human and veterinary medicine.

Subsect. B. PRINCIPLES OF THERMOTHERAPY

Thermotherapy, in its extreme form also known as *pyrexial treatment*[3519a, 3520a], has been recommended for a number of diseases in which a disturbance of the thermoregulation system seems to be an important causative or accelerating factor, for example rheumatic diseases, common cold, etc.

Pyrexial treatment is succesfully used to reduce excessive body weight. The body temperature is raised either by penetrating high-frequency currents (combined with insulation to minimize heat loss), or with an air cabinet containing moist air at temperatures of 42° C or more. In the first instance the skin temperature is lower than if the air cabinet is used. Also the pulse-rate increase, for any given level of body temperature, is less in cases of electro-magnetic induction.

Due to heavy sweating and water loss, patients may lose 3–5 kg in body weight during a 5 hours treatment. Prolonged treatment (10–27h) at 42° C has usually little effect. During the condition of hyperpyrexia, with temporary body temperatures of 105° F, several harmful physiological processes occur, *viz.*, the pulse rate may rise up to 160; the cardiac output may be increased; the circulation may be reduced to one third; the systolic blood pressure may be lowered to 60 mm in the erect position; the diastolic pressure may fall even to zero; acceleration of breathing causes alkalaemia; considerable losses of water and salt occur causing a 15% decrease in blood volume and increased haematocrit concentration.

Needless to say, patients who cannot support a considerable strain of the heart, or with a feeble kidney system, should never be subjected to such hyperpyrexia, which may be beneficial to others provided the treatment be not too protracted.

One of the most serious effects of pyrexial treatment is a state of collapse which may occur. The danger point can be determined according to Brown *et al.* by measuring the specific gravity of the blood plasma. During pyrexial treatment the serum protein values may rise from 6.9–8.5 g/100 ml. In this connection two points have to be considered before a patient is treated: (*i*) In some patients the normal protein level is already high. (*ii*) In winter the protein level (and specific gravity) is usually higher than in summer. According to Brown a person can stand a pyrexial treatment during 10–20 hours provided he is given orally 1 g of sodium chloride and 500–600 ml of water/h. However, under these conditions the weight loss is considerably reduced.

Less drastic treatments can be applied by causing the patient to inhale warm dry air (at the same time stimulating nasal secretion) and by giving him warm baths. The latter has a particularly favourable effect in the case of persons suffering from an overstimulated orthosympathetic nervous system due to heavy stress. Usually a pronounced drop in pulse rate occurs shortly after the bath and a decrease in average 17-KS secretion may be observed the next day. The extensive vasodilatation and increased peripheral blood flow eases some rheumatic complaints. Immediately after the bath, the patient should stay in bed under a blanket, as a preventive against chilling. Apart from these direct physiological effects, patients with a poorly functioning thermo-regulation system, find alleviation from remaining for many hours a day in an insulated environment of constant comfortable temperature (and infra-red radiation) and humidity, on all sides of the body, without any draught.

Subsect. C. PRINCIPLES OF HELIOTHERAPY

The principles involved in the treatment of patients with excessive solar radiation were reviewed by Ellinger on pp. 336–347. A summary of the main conclusions was given on pp. 450–451.

It was pointed out on p. 643 that excessive solar heat radiation can be found near the sea coast and at high altitudes near snowfields, because of intensive reflection. The differences in ultraviolet spectrum and intensity between high and low altitude areas were discussed on p. 339. For those clinical cases requiring intense ultraviolet radiation a helio course at high altitude is recommended, while strong infrared radiation can also be obtained on the sea coast, the effect of which on vasodilatation and peripheral overstimulation is usually reduced because of the greater air turbulence along the coast.

Excessive ultraviolet irradiation affects the development of micro-organisms, gastric secretion, blood pressure, haemoglobin values, calcium, phosphate and vitamin D level, protein metabolism, thyroid functioning, etc. (see p. 567); therefore, different heliotherapeutic treatments should be suggested to suit the specific complaints of the patients.

On p. 504 it was pointed out that most physicians agree that lung tuberculosis and serious chronic bronchitis should not be treated with intensive heliotherapy.

In normal healthy persons, heliotherapy usually strengthens the general resistance, but excessive solar irradiation, to which so many people like to expose their bodies these days, may have serious consequences (*e.g.* skin cancer), as already stressed on p. 481.

Subsect. D. CLIMATIC CHAMBER TREATMENTS

1. *General Construction and Physical Principles Involved*

by

J. D. FINDLAY and J. A. MCLEAN

Introduction

The use of climatic chambers as research tools by both human and animal physiologists is becoming increasingly widespread for studies in thermoregulation, adaptation to climatic stress and for therapeutic treatments.

A climatic chamber may be defined as an enclosure in which all the factors which describe any given climate may be reproduced and controlled. These factors are air temperature and humidity, wind velocity, temperature of nearby surroundings, solar radiation, ionization, precipitation and barometric pressure and provision for varying all of these in accordance with diurnal and seasonal fluctuations.

In practice it is seldom possible to include all these features in the design of a climatic chamber and the definition must be widened to include many chambers where some of the factors are neglected. Respiration calorimeters and pressurized chambers (to be discussed on pp. 636–642) which thus frequently fall within the broader definition are considered to be outside the scope of the present discussion and are therefore not included here.

The design of a climatic chamber intended for research purposes is further complicated by the nature of the physiological measurements that are to be made in it. These may include the measurement of total heat production and the measurement and partition of heat loss into its various channels of radiation, convection, conduction and evaporation both from the skin and from the respiratory tract. Other factors which inevitably influence design are the need to maintain the concentration of carbon dioxide and other gaseous excreta in the air below a maximum acceptable level, the need to avoid excessive noise from air movement and machinery and consideration of both capital and running costs.

The design of a climatic chamber is thus influenced by many considerations the claims of which are often mutually conflicting; moreover there are a variety of ways in which the many requirements may be met.

Air circulation

In order to maintain uniform temperature and humidity throughout a chamber some form of air circulation is required. In the simplest systems a propeller-type fan stirring the air in the room may be sufficient, but this does not give uniform air distribution. For close temperature control it is necessary to circulate air through a fairly large room at a rate of not less than one air change per minute. Usually it is wasteful of heat to draw such a large quantity of air from the atmosphere and return it again to the atmosphere after a single passage through the room and it is nearly always preferable to recirculate the air round a closed circuit comprising the chamber and the conditioning equipment joined by suitable ducting.

Fresh air must be admitted to the system at some point in order to avoid an excessive concentration of carbon dioxide. The increase in the percentage carbon dioxide concentration of chamber air over that of fresh air may be calculated as:

$$\frac{\text{Weight of } CO_2 \text{ added by subjects per unit time}}{\text{Weight of fresh air entering system per unit time}} \times 100$$

The quantity of fresh air required to maintain a reasonably low level of carbon dioxide is frequently small and for many simple chambers no provision need be made as leaks give adequate ventilation, or at most a simple ventilation shaft may be required. If a fresh air fan is required its position is not very important if, as is usual, the quantity of fresh air delivered is small compared with the total volume of air being circulated round the system, but it is generally convenient to site it so that it delivers air into the system between the point of extract from the chamber and the conditioning equipment. An axial flow type fan is often sufficient for delivering fresh air but a centrifugal fan may be required if the fresh air supply has to overcome a large static pressure. It is often possible to avoid the need for a fresh air fan by suitable duct design so that the main circulating fan draws part of its air from outside or by fitting vanes which accomplish the same result.

The main circulating fan will generally be of the centrifugal type and it should be mounted so that it does not transmit excessive noise or vibration to the rest of the system. This is done by making canvas connections between the fan and ducting. The fan and ducting should be large enough to avoid noise, and sharp bends in the ducting should be avoided since these, in addition to creating noise in themselves, increase the pressure against which the fan has to work, so increasing fan noise. Air velocities in ducts should not exceed about 1000 ft./min (300 m/min).

To ensure uniform distribution of the circulating air in the room, inlets may be fitted with baffles, grilles or louvres, many varieties of which are obtainable commercially, some having directional properties.

By these methods it is possible to design an air circulation system which gives good air distribution throughout the chamber and yet results in room air velocities being nowhere greater than 50 ft/min (15 m/min) thus approximating to still air conditions. If, however, high winds of known velocities are required it is necessary to construct the entire chamber as a wind tunnel using a large axial flow fan of special design. For some purposes however, it may be sufficient to produce high air velocities by mounting auxiliary fans inside the chamber.

Insulation

Insulation is necessary firstly to avoid loss of heat and secondly to maintain surface temperatures near to air temperature. If surface temperatures are required to be very close to air temperature special means of maintaining this condition are required and these are discussed later. If it is sufficient to maintain surface temperature to within only a few degrees of air temperature insulation of the surface is sufficient.

TABLE 42

THERMAL RESISTANCE OF VARIOUS BUILDING AND INSULATING MATERIALS

Material	*Density*		*Thickness*		*Thermal resistance*	
	lb/ft³	*kg/m³*	*in.*	*cm*	*°F ft²/h/B.t.u*	*°C m²/h/kcal*
Common brick	—	—	4.5	11.5	0.9	0.18
Concrete:						
heavy aggregate	140	2240	1	2.5	0.08	0.016
light aggregate	60	960	1	2.5	0.5	0.10
Timber	35	560	1	2.5	0.9 – 1.3	0.18 – 0.27
Compressed cork	14	224	1	2.5	3.0	0.62
Mineral wool	4	64	1	2.5	3.5	0.72
Expanded ebonite	4	64	1	2.5	5.0	1.03
Vertical airspace bounded by aluminium foil	—	—	—	—	2.2	0.45
Air to normal wall interface	—	—	—	—	0.9*	0.18*

* See text.

The thermal resistances of various building and insulating materials are given in Table 42. The value for an air to wall interface depends very greatly on the amount of air movement near the surface and the figure given is an approximate one that is representative of typical heat transfer to the walls of a climatic chamber in which conditions approximate to still air. The total heat loss through an insulated wall is given by the product of the surface area and the difference between room and ambient temperatures divided by the total thermal resistance. The total thermal resistance is the sum of the thermal resistances of the various layers of material forming the heat transfer barrier from within the room to the outside. For example, an 80 ft^2 (7.4 m^2) wall consisting of 4 inches (10 cm) of mineral wool (resistance 14 °F ft^2/h/B.t.u. or 2.9 °C m^2/h/kcal) retained by a 4.5 inch (11.5 cm) brick wall (resistance 0.9 °F ft^2/h/B.t.u. or 0.18 °C m^2/h/kcal) in a room maintained at 20 °F (11 °C) above ambient temperature will lose $(80 \times 20) / (14 + 0.9 + 0.9) = 100$ B.t.u./h (25 kcal/h). Most of the temperature gradient of 20 °F (11 °C) occurs through the insulating material, but of the total temperature drop the proportion that exists across the air-to-surface interface is equal to the proportion of the thermal resistance of the interface to the total thermal resistance, in this instance 0.9/15.8 or 5.7%. The difference between wall temperature and air temperature is thus $0.057 \cdot 20 = 1.1$ °F (0.6 °C). It must be stressed that this calculation of surface temperature is very approximate. Agreement between wall and air temperature would be much improved if air movement inside the room were greater and wall temperatures would rise very noticeably if an occupant of the room were standing close to the wall and radiating heat to it. Such calculations are nevertheless useful in giving a rough guide to the closeness of surface and air temperatures for a given amount of insulation.

Any of the insulating materials given in Table 42 are suitable for wall insulation. Still air is one of the best insulating materials of all but an air gap loses much of its insulating efficiency due to convection currents which occur unless the air gap is divided into a series of small compartments. Mineral wool, expanded ebonite, expanded polystyrene, foam rubber and many other insulating materials owe their efficiency to the fact that they are composed of millions of minute air pockets. Insulating materials are of necessity light and not mechanically strong and therefore normally require a supporting structure on both sides. The outer retaining wall and ceiling of a climatic room may be made of a timber framework covered with hardboard or for stronger structures of brick or concrete. The inner wall is merely a lining which presents a smooth surface and acts as a vapour seal to prevent moisture entering and destroying the insulation; a thin metal is suitable, usually aluminium alloy and allowance must be made for expansion if the temperature is likely to vary over wide limits. Joints may be embedded in a plastic sealing compound. For floor insulation compressed cork is suitable and it is usually necessary to protect the surface with a hard plastic or rubber lining. If the floor is to carry heavy weights, a concrete covering is required. If the room is to be subjected to temperatures below freezing point stringent precautions must be taken to ensure that no moisture vapour can enter any concrete or brickwork otherwise serious structural damage may result.

Doors, windows, service entry points and drains all represent weak spots in the overall insulation and special precautions may have to be taken. If space permits, an airlock as small as possible yet large enough to accommodate any subject or animal entering or leaving the room should be included in the design. Windows should be multiple glazed and the air gap between panes must be dried-out and vapour sealed or condensation may obscure the window when working at low temperatures. If the humidity is high, condensation is liable to occur on the window surface inside the chamber and this may be overcome by using a pane of glass with a fine wire heating mesh incorporated in it. Electric wiring, water pipes and leads to measuring instruments that must pass into the room may be brought in via tubes made from insulating material that are inserted permanently through the wall at the time of building. The leads and pipes may be passed down the centre of the tube, both ends of which are then sealed off to form an air gap within. Drains should be made if possible from plastic piping and fitted with conventional traps for sealing purposes.

Surface temperatures

If surface temperatures are required to be very close to air temperature, metal curtaining may be used. This in its simplest form merely consists of hanging large sheets of thin polished aluminium within a few inches of the walls. Room air is allowed to circulate behind these sheets, and the true wall facing the sheet is also of polished aluminium so that radiative heat exchange between the two surfaces is reduced to a minimum and the false wall or curtain is heated directly both in front and behind by room air. The face of the false wall that is presented to the room may be dulled or painted if a non-reflecting surface is required. This system greatly reduces the effect of radiation from subjects within the room on surface temperatures especially if a good degree of circulation is maintained behind the curtaining. The mere hanging of such curtaining in an existing room helps considerably to improve agreement between air and surface temperatures but if full benefit is to be obtained from the system the curtaining should be built-in permanently and the air circulation arranged so that the entire air supply to the room is passed through the cavity so formed between the inner and outer walls before it enters the room itself. A light false wall or curtaining system also allows surface temperatures to change more rapidly due to reduced heat capacity and therefore allows them to follow more closely changes such as applied diurnal fluctuations in air temperature. The air supply can also be passed through the gaps between double window panes and double doors. It is essential that the false surfaces should have high thermal conductances and here the floor presents a problem since it must combine this property with strength.

Control of surface temperatures at room air temperature or at some desired different temperature may also be achieved by direct heating or cooling of the walls by means of piped liquid. Allowance for expansion of metal piping due to heat must be made during construction, and the filling between adjacent pipes and the wall surface must be made of heat conducting material while the space behind the piping must be insulated. Special radiating panels that can be heated or cooled by liquid are available commercially. Effective surface temperatures considerably in excess of air temperatures may be produced also by means of reflecting panels and heaters placed at suitable locations. It is possible in this way to produce an effective radiant temperature of the surroundings that is nearly uniform in all directions with only three or four localised heat sources[3526].

Solar radiation and precipitation

It is possible to simulate solar radiation in a climatic chamber by the use of a battery of incandescent and fluorescent lamps[3525]. The number and intensity of lamps to be used depends on the characteristics of the normal solar radiation of the district whose climate is to be simulated and only a rough approximation to the solar spectrum can be expected by this means. The proportion of infra-red to visible radiation given off by lamps is far greater than that in the solar spectrum and this can be allowed for to a certain extent by the use of glass filters. Special ventilation of the lamps is necessary to remove the large amount of heat given off.

Rain may also be simulated by the installation of roof sprays, the temperature of the spray water being suitably controlled.

Heating and cooling

The circulating air is most conveniently heated by means of electric heater elements and cooled by means of liquid cooled pipes fitted with fins. The cooling pipes can obviously also be used in conjunction with steam or heated liquid for air heating, but it is not normally practicable to use the same fluid for both heating and cooling, and the pipe system is more bulky than electrical heaters. Electrical heating is further far more efficient than pipe heating as the heat transfer is 100% efficient and there is no heat loss from the electrical leads whereas hot or cold liquid pipes leading to coolers require to be thermally insulated. Coolers employing tap water as the cooling liquid may be suitable for maintaining climatic chambers at or even a little below ambient temperature but if temperatures appreciably below ambient are required refrigerated liquid is essential. Brine is used when, as is often so, the cooling liquid has to be maintained below 32° F (0° C).

The total amount of sensible heat to be supplied or removed from the system, *i.e.* the sensible heating or cooling load Hs, is given by

$$Hs = I + Cs - Ps - A$$

where I is the heat loss from the chamber to the outside through the insulation of the chamber and any associated ducting and conditioning equipment. It can be calculated as previously described. Cs is the sensible heat loss by forced convection (B.t.u./h or kcal/h) from the system as a whole due to fresh air ventilation. Cs is approximately equal to the product of three quantities: the temperature difference between the chamber air and the fresh air (°F or °C), the rate of delivery of the fresh air into the system (ft.^{3}/h or m^3/h), and a constant (0.0185 B.t.u./ft.^{3} °F or 0.295 kcal/m^3 °C) which combines the density and specific heat of air and is applicable over a fairly wide range of ambient air conditions. I and Cs may be positive or negative. Ps is the sensible fraction of the heat loss of all subjects and animals contained in the chamber. A is the heat produced by auxiliary sources such as lights, radiating panels and fans, an estimation of which may be obtained from the wattage. Ps and A are always positive.

An approximate conversion of the sensible heating load so calculated to terms of the electrical heating power required may be obtained by multiplying the former expressed in B.t.u./h by a factor of $2.93 \cdot 10^{-4}$ (or expressed in kcal/h by a factor of $1.16 \cdot 10^{-3}$) to give heating power in kW.

Humidifying and dehumidifying

Humidification of the air is most conveniently achieved by the injection of steam, which may be raised in a number of ways. For small systems a heating element placed in a shallow trough of water, which is replenished as used to a constant level, forms a simple and convenient method, but it is slow in responding to a demand for steam. An improvement of this method is to drip water onto a revolving horizontal plate which thus throws a fine spray of water outwards onto a surrounding circular heating element. The heating element is wrapped in a cotton cloth which acts as a wick and retains only sufficient moisture to prevent damage to the element when the latter is switched on; excess moisture which falls off the element is collected in a drip tray. Both of the above methods result in the production of a considerable proportion of sensible as well as latent heat.

For larger systems steam may be raised in any form of steam boiler and stored under pressure ready for injection into the system via control valves. The final injection pressure should be kept low in order to avoid excessive noise. Another very convenient way of raising steam which lends itself to control is to have an electrode boiler connected to the ducting system via an open pipe so that the boiler is never under pressure and acts as an open kettle; the rate of steam generation may then be controlled by varying the water level in the boiler to cover more or less of the electrode surfaces as required.

Moisture may be removed from the air by dehydration, in which solid moisture absorbing materials such as silica gel or activated alumina are used alone, or by dehumidification involving condensation of moisture by cooling usually combined with a liquid dehydrating material such as calcium chloride brine. All dehydrating materials lose their efficiency as they absorb moisture and continuous regeneration is necessary. This may be done by circulating the dehydrating material on a rotating drum when solids are used or by piping when liquids are used. The dehydrating material passes first through the air stream to be dried where it absorbs moisture, then through a reactivator and finally through a cooler or heat exchanger before repeating the cycle. Reactivators for solid dehydrating materials usually consist of a chamber in which air from outside heated to upwards of 300° F (150° C) is passed over the material. The same method can be used for liquids but some of these may also be reactivated by boiling to remove the excess moisture. In the absorbing chamber the dehydrating material is made to present as large a surface area to the air stream as possible. For liquids this is done by spraying and passing the liquid over a network of pipes usually containing a liquid cooling agent.

The total amount of moisture vapour to be supplied or removed from the system, *i.e.* the latent heating or cooling load H_L is given by

$$H_L = C_L - P_L$$

where C_L is the latent heat loss by forced convection (B.t.u./h or kcal/h) from the system as a whole due to fresh air ventilation. C_L is approximately equal to the product of three quantities: the difference in vapour pressure between the air in the chamber and fresh air (in. Hg or mm Hg) the rate of delivery of fresh air into the system (ft.^{3}/h or m^3/h) and a constant (1.79 B.t.u./ft^3 in.Hg or 0.625 kcal/m^3 mm Hg). The constant combines the density of fresh air, the latent heat of vaporisation of water and a factor relating vapour pressure to humidity ratio, and is applicable over a fairly wide range of ambient conditions. C_L may be positive or negative. P_L is the insensible fraction of total heat loss from all subjects and animals contained in the chamber.

An approximate conversion of the latent heat load so calculated to terms of the weight of steam required may be obtained by multiplying the former expressed in B.t.u./h by 0.00092 to give steam required in lb./h (or expressed in kcal/h by 0.00165 to give steam in kg/h).

It must be stressed that these equations for estimating sensible and latent heat loads are only approximate, but they can readily be used for making rough estimations in the temperature and humidity ranges likely to be met with in climatic chamber construction. If accurate estimations are required resort should be made to suitable psychrometric charts. The equations are however sufficiently accurate to give estimates as to the probable size of heaters, coolers and quantities of steam that may be required. It should be appreciated that the various heaters and coolers do not act entirely as intended and that interactions between them will almost certainly occur. Thus a certain amount of latent cooling (condensation) may frequently occur in sensible coolers and sensible cooling in latent coolers; also steam injection invariably results in the addition of sensible as well as latent heat. For these reasons and to allow for errors of load estimation and for extreme weather conditions generous safety factors should be allowed.

Control systems

A wide range of control systems exist for regulating the amounts of sensible or latent cooling and heating, and these control systems may be actuated by various temperature and humidity sensing elements. Hair or other expansion hygrometers may be used for humidity sensing but are generally subject to hysteresis and not very reliable except for control at a permanent relative humidity setting. Most other humidity sensing elements are devices which hold themselves at some temperature which is related to air humidity; these include wet bulb thermometers and dewpoint thermometers. Wet bulb thermometers are inconvenient in that they have to be kept supplied with distilled water, their wicks require frequent attention and their humidity settings are affected by alterations in air temperature. A convenient form of dewpoint thermometer that is commercially available is the Foxboro-Yoxall Dewcel. This is a device that maintains itself at a temperature (not actually the dewpoint temperature) which is dependent solely on the absolute humidity of the air. The sensing of humidity is thus reduced by wet bulb and dewpoint thermometers to the sensing of temperature. Temperature sensing elements include bimetallic thermostats and mercury-in-glass contact thermometers, both of which are suitable for on-off control systems, and also resistance thermometers, liquid-in-metal expansion thermometers, thermocouples and thermistors all of which lend themselves to use in proportional controllers.

The simplest form of controller is the on-off type where, for example, a heater is switched on or off depending upon whether the air temperature is below or above that required. On-off controllers are suitable for simple systems where closeness of control is not important and are generally combined with manual or semi-automatic means of regulating some auxiliary heaters so that only a small proportion of the total heating power is switched on and off by the controller. Proportional controllers with integral action are those in which any departure in temperature from the set conditions is compensated for by a proportional alteration in the amount of heat supplied. These give sufficiently close control for most purposes. Still closer control is sometimes possible if derivative action, which modifies the amount of heat supplied according to the rate at which the temperature is changing, is also included. Proportional controllers may be electronic or pneumatic in operation and many are commercially available. They usually include an automatic printing or graphic indication system which gives a permanent record of the temperature or humidity being controlled. Some controllers can be fitted with a device which enables the user to vary conditions within a chamber according to a pre-set time schedule, for example to simulate diurnal variations.

The output from the controller takes the form of electrical or pneumatic signals which operate relays, valves or motors and so switch on and off or otherwise regulate the various heaters, coolers, humidifiers and dehumidifiers. Electric heaters may be energized in proportion to the output signal from the controller via a motorised variable transformer, or may be divided into a series of banks which are switched on in sequence as the load increases and off in the reverse order as it decreases. The supply rate of steam may be controlled by the position of a regulating valve as can be that of brine to coolers. Alternatively the rate of steam generation from an electrode boiler may be increased by a pump which raises the water level in the boiler or reduced by opening a valve to drain the boiler. Control of the amount of cooling or dehumidification may also be achieved by adjustment of movable dampers which divert more air through coolers and less through by-pass ducts or *vice versa*.

For simple systems it may be sufficient to use a commercial unit air conditioner. This consists of a cabinet equipped with fan, heating and sometimes cooling equipment and control system which draws air in at one end and passes it out conditioned at the other. The unit may be purchased complete and installed in almost any room thus converting it into a simple climatic chamber.

Refrigeration

For the supply of cold brine to coolers and dehumidifiers a refrigeration system is necessary. The cold brine may be stored in a tank and the return brine supply from the coolers passed through the evaporator of the refrigeration plant, or for smaller systems an expansion coil for evaporating refrigerant fluid may be immersed in the brine tank. It is sometimes possible to feed the refrigerant fluid directly to the coolers and heaters. The total amount of refrigeration required may be estimated from the combined maximum sensible and latent cooling loads under the most adverse conditions of running the chamber at minimum temperature and humidity on a hot summer day. Allowance must also be made for heat losses from brine pipes connecting the coolers to the refrigerating plant.

A practical climatic chamber

As an example of a climatic chamber Fig. 94 shows the schematic layout of the Precision Climatic Chamber at the Hannah Dairy Research Institute in Scotland. The chamber (A) designed to accommodate one adult cow and measuring equipment, has internal dimensions $18 \times 12 \times 10$ ft. high ($5.5 \times 3.7 \times 3.0$ m) and consists of an outer and inner shell. The outer shell is a brick and concrete structure with a 5 in. (13 cm) insulating layer, composed of mineral wool for the walls and ceiling and compressed cork for the floor, and an internal lining of aluminium sheet. The inner shell is made of aluminium sheet for the walls and ceiling and steel sheet covered by reinforced concrete and asphalt for the floor. The inner shell is held in place by insulating blocks mounted on the outer shell so forming a 3.5 in. (9 cm) cavity (B) into which air is delivered at a rate of 7000 ft.^{3}/min (200 m^3/min) by the main fan (C). The air passes all round the inner shell and most of it is exhausted into a duct under the floor, but a proportion of it (2500 ft.^{3}/min or 70 m^3/min) enters the chamber itself via a baffled slot 3 ft. (0.9 m) above floor level which extends all round the room. The air leaves the room via a duct in the centre of the ceiling which joins with that from the under floor cavity; the recombined air stream being joined by fresh air, delivered at a rate of 120 ft.^{3}/min (3.4 m^3/min) from fan (D) and passed through the coolers (E and F) back to main fan (C). Stale air passes from the room either directly to outside via an auxiliary duct (G) or it may be by-passed through an air-lock which gives access to the room. Air movement inside the chamber is less than 60 ft./min (18 m/min) except close to the walls.

The electrical air heater (H) has a total capacity of 24 kW arranged in six banks, two of 3 kW and four of 4.5 kW, and is situated with the steam injection nozzles (I) in the duct just after the main fan (C). The sensible heat cooler (E) consists of finned tubes through which calcium chloride brine is circulated. The latent heat cooler (F) is of similar construction but in addition brine from an auxiliary system is continuously sprayed over the tubes

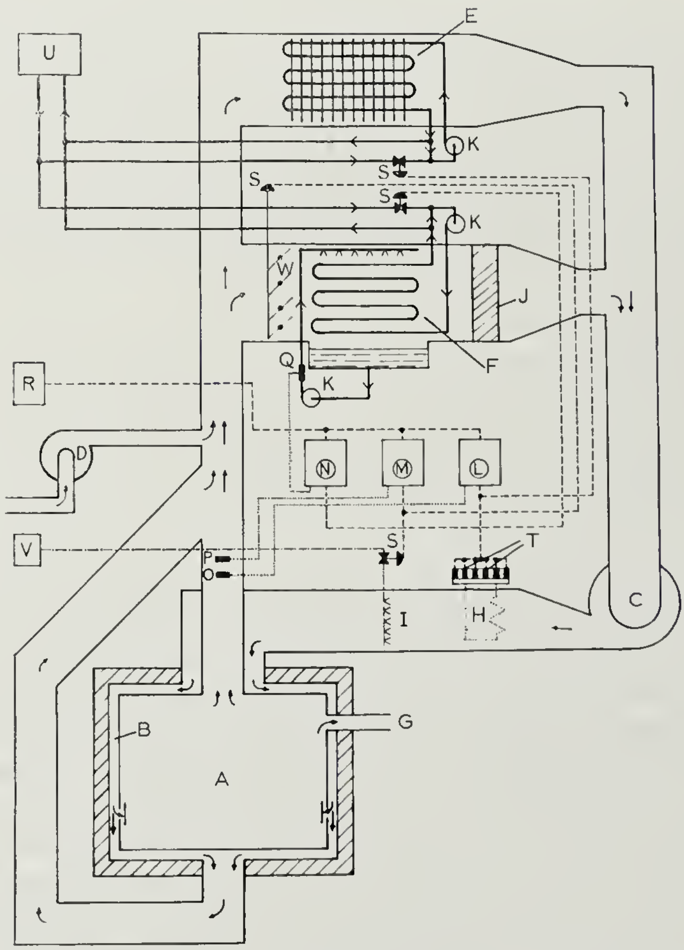

Fig. 94.
Schematic diagram of the Precision Climatic Chamber at the Hannah Dairy Research Institute. A: chamber; B: inter-wall cavity; C: main circulating fan; D: fresh air fan; E: sensible heat cooler; F: latent heat cooler; G: stale air exhaust duct; H: heater banks; I: steam injection nozzles; J: spray eliminators; K: brine pumps; L: air temperature controller; M: air humidity controller; N: spray brine temperature controller; O: air temperature sensing element; P: air humidity sensing element; Q: brine temperature sensing element; R: compressed air supply; S: pneumatic modulating valves; T: pressure switches; U: refrigerated brine supply; V: steam supply; W: air dampers.

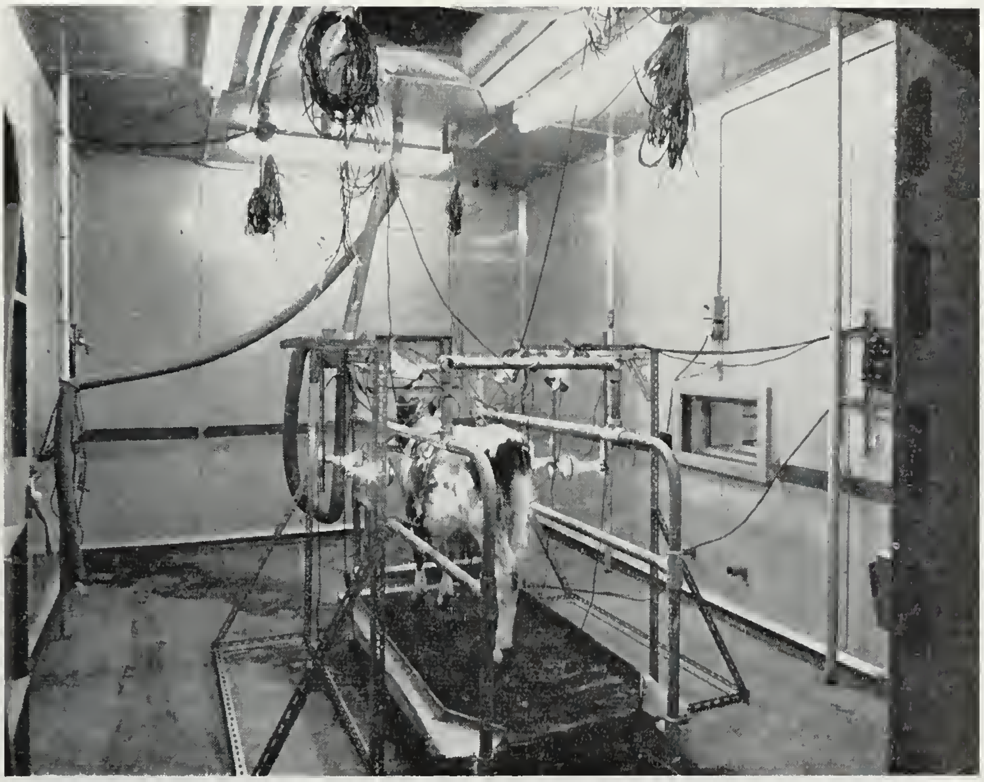

Fig. 95.
A calf undergoing experiment in the Precision Climatic Chamber at the Hannah Dairy Research Institute.

and collected in a drip tray at the base of the cooler. Droplets of spray brine are prevented from being carried through the rest of the ducting system by glass wool eliminator mats (J) situated immediately after the cooler. Brine is circulated through the coolers by pumps (KK).

There are three controllers, one for air temperature (L), one for air humidity (M) and one for spray brine temperature (N). They obtain their information from a resistance thermometer (O) and a Foxboro deweel (P) both situated in the extract duct of the chamber and from a resistance thermometer (Q) in the spray brine supply line. The controllers, fed with compressed air from supply (R) operate pneumatic valves (SS) and the pressure switches (TT) so controlling rates of flow of air, brine or steam and the operation of the heaters. Air temperature is raised by sequential operation of however many heater banks are required, by the pressure switches (TT) or it is lowered by allowing a suitable quantity of brine at 18° F (−8° C) from the refrigerating system (U) to enter the circulation of the sensible

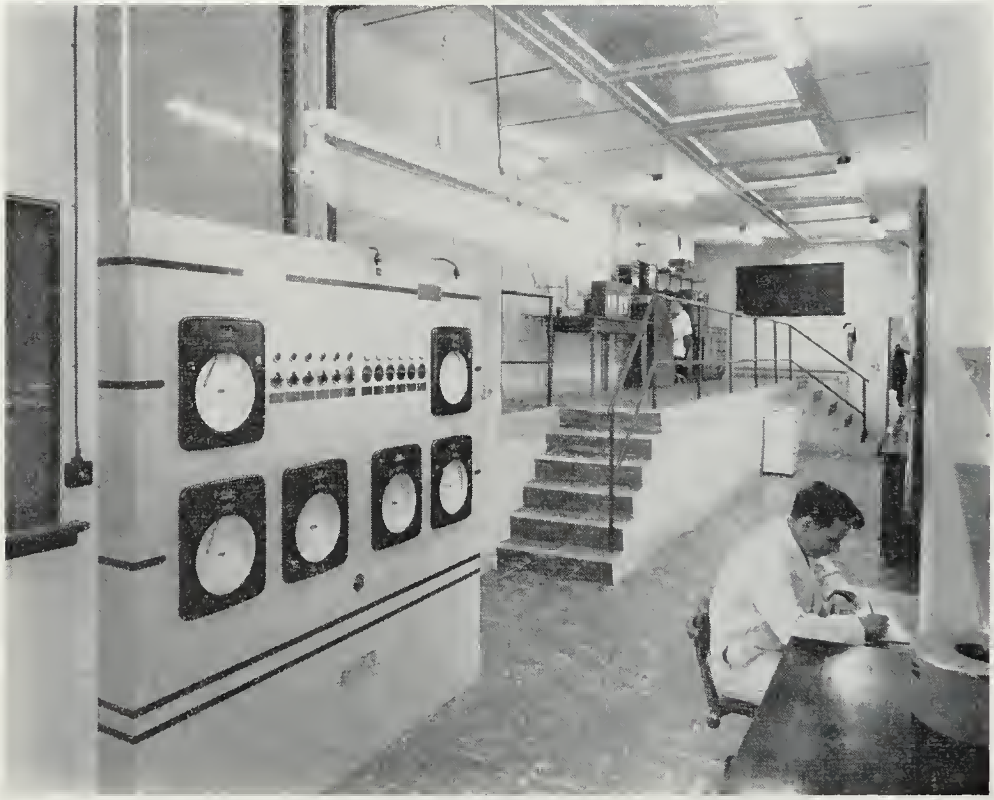

Fig. 96.
The observation room for the climatic chambers showing some of the measuring equipment.

heat cooler (E). Air humidity is raised by injection of steam from supply (V) or lowered by operation of the dampers (W) which allow some of the air-stream to be diverted from the sensible to the latent heat cooler. Spray brine temperature is cooled to a suitable level, chosen according to the conditions required, by injection of cold brine from the refrigeration system (U) into the circulation through the tubes of the latent cooler (F), *i.e.* not directly into the spray system which is an entirely separate brine supply. The concentration of the spray brine is maintained at a sp. gr. of 1.23 by an auxiliary control system not shown, which passes the brine to a concentrating vessel to maintain a constant level in the drip tray. The concentrating vessel is steam heated to 235° F (113° C). Cold brine going from the latent cooler to the concentrator and returning hot brine pass through a heat exchanger.

In the building containing this Precision Climatic Chamber there is also a larger climatic chamber. The refrigeration system, which is common to both, is a dichloro-difluoro-methane system powered by two 15 h.p. com pressor motors and has a total capacity of 170,000 B.t.u./h (43,000 kcal/h).

The range of operation is from 32–140° F (0–60° C) air temperature. Minimum humidity is less than 32° F (0° C) dewpoint temperature, rising to 64° F (18° C) dewpoint temperature at air temperature of 140° F (60° C); maximum humidity is saturation below 68° F (20° C) air temperature falling to 95% saturation at 113° F (45° C) and approximately 2.76 in.Hg (70 mm Hg) vapour pressure above 113° F (45° C). Air temperature, surface temperatures and dewpoint temperature are all controlled to within ± 0.5° F (± 0.3° C) over the entire range.

The other chamber is of the same height but has approximately twice the floor area. Its construction is similar to that of the Precision Chamber except that the inner shell is omitted and the air circulation simplified accordingly. The range of operation is the same but the accuracy of control of air and surface temperatures is less (± 4° F or ± 2.2° C).

Fig. 95 shows an animal undergoing experiment in the Precision Climatic Chamber, and Fig. 96 shows the observation room with some of the measuring equipment associated with both rooms.

The contract for the installation was carried out by Messrs. J. & E. Hall, Ltd., Dartford (England). The control equipment described was supplied by Messrs. Foxboro-Yoxall, Ltd., Redhill, Surrey (England). The installation was completed in 1959. It is used for studies in the physiology of heat regulation and adaptability to climatic stress of cattle.

Several climatic chambers of varying complexity are being built or are in existence throughout the world but very few have been described in detail. Amongst those of which descriptions have been published are the ones at the University of Missouri[3524], the John B. Pierce Laboratory of Hygiene, Newhaven, Conn.[3527], the University of Edinburgh[3523], and the former climatic room at the Hannah Dairy Research Institute[3522].

2. *General Physiological Principles involved in Climatic Chamber Treatment*

by

H. NÜCKEL and G. LINCKE*

General considerations

Climatic chamber treatment comprises the therapeutic applications of

* At the author's request, on 30th April 1960, Dr. H. Nückel, with the assistance of Dr. G. Lincke, published an extensive review of this whole problem in the *Intern. J. of Bioclimatol. and Biometeorol.*, *4*, 1960, under the title *Klimakammer Therapie*. In the following pages a brief English summary is given of this review. For further details the reader is referred to the original publication. A number of references related to the subject and compiled by Nückel Lincke and Tromp is given in the reference-list (the numbers [3528–3558]).

an artificial climate, usually created in a specially constructed chamber or room of limited dimensions. This artificial climate usually differs in one or more components from the local natural climate.

So far, of the various climatic and meteorological factors only a restricted number have been applied in climato-therapy. They are: aero-colloids, atmospheric pressure, temperature, humidity, air movement, ionisation, potential gradient, infra-red and ultraviolet radiation.

A well-known method of climatic chamber treatment, applied more especially in the tropics, is *air-conditioning*, the principles of which were discussed on pp. 244–245. The main purpose of this kind of treatment is to create that specific micro-climate which is most agreeable to the people living in it. However, most climatic chamber treatments aim at creating an artificial condition for the main purpose of initiating a specific stress condition which affects the human body either specifically in certain organs or non-specifically. In the latter case the body as a whole is stimulated.

For practical purposes the various climatic chambers can be classified into two groups: climatic chambers with only one varying meteorological component (usually only a variation in aero-colloids) and those with more than one varying component (in particular, variations in atmospheric pressure).

Climatic chambers with only one varying meteorological component (variation in aero-colloids)

The various trace substances, aerosols and air-polluting substances (organic and inorganic particles and chemical pollutants), which together form the aero-colloid of the local climate, were reviewed on pp. 88–148.

Assuming that, under conditions of total rest, the amount of inspired air during each respiration amounts to 0.5 l and the breathing frequency is 15–20/min, the total amount of inspired air/min would amount to 7.5–10 l or 10,000–15,000 l/day. During muscular activity it is considerably more; *e.g.*, a coal miner may have a breathing volume of 24 l/min. In the course of $7^1/_2$ hours' work, about 10.8 m^3 of air will pass through his lungs, with a dust content of 75 mg/m^3. It has been estimated that of particles $< 5\ \mu$, about 810 mg of dust will penetrate into his respiratory tract only during these $7^1/_2$ working hours. It is therefore evident that a change in aero-colloids may be highly beneficial, both prophylactically and therapeutically. For this purpose two types of climatic chambers have been introduced, chambers free from allergens and aerosol-chambers.

(a) Climatic chambers free from allergens

This type of chamber was introduced for the first time in 1924 by Storm van

Leeuwen[1910, 1915], who believed that asthmatic attacks were mainly caused by allergens in the air. The patients were placed in allergen-free rooms of $2.5 \times 2.5 \times 3$ m, air being admitted into them through a funnel 35–40 m in height. After the air had been cooled and further cleansed, it was warmed up again and introduced into the room.

Favourable effects are also obtained in these rooms during the hay-fever season (see p. 462).

(b) Aerosol chambers

The four different types of aerosol chambers briefly discussed on p. 605 were the *acid-spray chamber,* the *ultrasonic spray chamber,* the *salt-water spray chamber* and the *diapneumotherapeutic chamber.* In these various types of aerosol chambers the main purpose is to change the natural aero-colloid by introducing therapeutic aerosol sprays. Depending on the physical properties of the aerosol, the droplets will penetrate into the respiratory tract at different depths (see p. 104). Smaller concentrations of aerosols are required than of orally applied drugs, as the latter have first to be absorbed by the intestines before a small fraction of the consumed drug reaches the bronchi. For example, 75 γ of aludrin cause a bronchial spasmolysis which can only be achieved by an orally consumed tablet in a concentration of 20 mg. Also, various harmful indirect effects on the heart, stomach, etc. can often be eliminated by using aerosol inhalation instead of drug tablets.

(1) *Acid spray-chambers.* Kapff (see p. 605) introduced a special acid spray consisting of 82% of formic acid ($HCOOH$), 3% of acetic acid (CH_3COOH) and 1% propylene glycol ($CH_2OHCH_2CH_2OH$). The fluid evaporates from special evaporation dishes as a result of an air current created by a ventilator. By changing the rotational speed of the ventilator and the distance to the dishes, the concentration of acids in the air can be regulated. Each treatment takes about 10–20 minutes and is repeated three times a week, but can be increased to twice a day if necessary. In certain spas (see p. 648) very large acid spray chambers are used, *e.g.* $7 \times 5 \times 4$ m which can hold 15–20 people at a time.

The effect of acid sprays is explained as follows: (*i*) Electron microscopic studies by Low and Dettmer suggest that the receptors for acid vapour stimulation are located in the alveolar wall of the lungs. The acid vapours make the alveolar cells more globular and, as a result, the blood capillaries in between are directly exposed to the air current which facilitates the oxygen exchange between alveolar air and blood. During various chronic conditions of hypoxia (*e.g.* pulmonary emphysema of old people, various lung-dust diseases such as silicosis, etc., see p. 113) such acid-spray treatments bring considerable relief for several hours. (*ii*) The pH of the aerosol also affects the permeability of membranes, phagocytosis (see p. 99) and so on. (*iii*) Formic acid and acetic acid are able to dissolve the lipids and this facilitates penetration into the cells and the destruction of bacteria. These various properties of acid aerosols increase the local resistance to infections (see p. 511) like the common cold, catarrhs of the upper respiratory tracts.

(2) *Ultrasonic spray chambers.* Ultrasonics facilitate the production of stable aerosols. For rooms of 50 m³ an energy of only 20 W is required. Usually round chambers (4.5 m in diameter and 3 m in height) or square chambers (4 × 4 × 3 m) are used with 2–6 ultrasonic units. About 15 people can be treated at the same time for 20 minutes, followed by a 15 minute period of extensive cleaning of the air before a new group enters the chamber. During an eight-hour working day about 150 patients can be treated with different aerosols. The size of the aerosol droplets depends mainly on the frequency of the ultrasonic unit. For bronchospasms and asthmatics a frequency of 2.7 MHz is recommended, forming droplets of 0.5–1.4 μ. As a result the total amount of aerosol penetrating into the lungs is 300 times more than in the case of normal evaporated fluids with droplets larger than 5 μ. For the same reason, concentrations of only 0.2‰ aludrin and isolevin aerosols are required in ultrasonic sprays, as against 1% in the case of ordinary evaporation, which also explains why undesirable complications are less apt to occur in aerosol treatment. A further great advantage of the ultrasonic chamber is that substances can be mixed which would normally interact in a solution. Adrenaline, for instance, can be sprayed without being oxidised immediately, as would otherwise happen. Various ultrasonic units are used simultaneously to spray a number of different aerosols at the same time. For further details concerning this method we refer to the original article by Nückel and Lincke.

(3) *Salt water spray chambers.* These are successfully used against catarrhs of the upper respiratory tract. The aerosol droplets should vary between 10 and 50 μ. The evaporators use compressed air of 2 atm., which passes through a salt-water solution, causing a dense fog in the chamber with a visibility of about 1 m. The following physiological effects have been observed: (*i*) A calming effect on ciliary activity. (*ii*) Hypertonic aerosol solution (see p. 651) reduces the swelling of the cells caused by an infection, whereas a hypotonic fog increases the complaints of bronchitics. A hypertonic aerosol also increases the bronchial secretion and lowers the viscosity of the sputum, which can be more easily expectorated. Salt-water sprays are therefore recommended for various laryngo-tracheal bronchitic complaints, often in combination with etherial oils (see p. 610).

(4) *Diapneumotherapeutic chambers.* The aerosol chamber is used for the indirect treatment of various parts of the body through the healthy respiratory tract, which acts only as an absorption organ. Aerosols with droplets of 0.5–5 μ are recommended. Usually very large rooms are used, for example in child clinics, where the children can play in an atmosphere containing these aerosols. Guassardo applied aerosols of salicylic acid and salicylates for the treatment of children suffering from rheumatic diseases. In other clinics drugs stimulating general metabolism or antibiotics have been recommended, although experiments with penicillin have shown a gradual decrease in effect. In certain psychiatric clinics, sedative drugs have been used in such aerosol chambers. Only drugs which dissolve as anions seem to be effective, because they penetrate through the tissues into the lymphatic lymph channels and blood capillaries, whereas cathodic drugs are attracted by the protein micelle bodies of the cells and do not reach the blood stream.

Climatic chambers with more than one varying meteorological component (in particular, variations in atmospheric pressure)

Whereas the human body is fairly well adapted to the continuous changes in temperature, humidity, radiation, air movement and ionisation of our environment, the average person has not become habituated to rapid changes in atmospheric pressure. It is therefore not surprising to find that this form of environmental climatic stress has the greatest physiological effect. It explains why the term "climatic chamber" is often used for a "low pressure chamber".

If many persons are congregate in the same chamber, there is a detectable reduction in oxygen and increase in CO_2, apart from other volatile substances released by the body and clothes. A continuous renewal of air is therefore required, which should, if possible, be about 20 m³/h or 333 l/min/person. The complete exchange should take place, if possible, 10–20 times/h. The volume V of the chamber in m³ required for satisfactory air renewal is therefore

$$V = \frac{a \cdot n}{b}$$

where a = air exchange per person/h in m³ (= 20); b = number of air exchanges/h (= 10) and n = number of persons.

Though the fresh air may permissibly be more than 20 m³, precautions should be taken against the creation of air currents of more than 0.3 m/sec, as these would cool off the patient uncomfortably. Whereas in the case of low-pressure chambers with a pressure equal to 4000 m a patient can usually be brought down to sea level in 20 minutes and can leave the chamber, with high-pressure or pneumatic chambers it may take an hour or more. As the patient has to stay at least 30–45 minutes under the minimum or maximum pressure conditions, one pneumatic chamber treatment may take $1^1/_2$ hours. This makes it necessary to have large chambers, comfortable chairs and big, transparent windows lest the patients be overcome by claustrophobia. The temperature and humidity conditions should be so regulated that the patients feel neither too warm nor too cold. Obviously, the temperature-humidity conditions have to be adapted to the seasons, the prevailing weather and the specific needs of the patients (see p. 230).

In Bad Lippspringe in Germany the wall of the chambers is usually 19° C, the R.H. either 35% with room temperature 22° C (in winter) or 25.5° C (in summer), or 50% with room temperature 21° C (in winter) or 24.5° C (in summer). The air movement is about 0.1 m/sec. The air passes electrically heated wires, causing a slight surplus of negative ions, the effect of which has been discussed on pp. 353–365.

Patients should change their clothes before entering the low-pressure chamber because various vapours, sweat and bacteria attached to clothes and shoes may escape into the air at low pressure, making it unpleasant for other persons in the same room.

(a) High-pressure or pneumatic chamber

The first therapeutic chamber, used both for high and low pressure purposes, was constructed in 1664 by Henshaw and was known as "Domicilium". In 1841 von Triger discovered the caisson. This was followed by a series of physiological studies in 1863 by Vivenot in Vienna and Erlangen and by von Liebig in 1888 in Bad Reichenhall. The high-pressure chambers are often made of reinforced concrete with a special sluice system. At Bad Reichenhall they are used both for high- and low-pressure experiments.

(1) *Physical factors involved.* In the high-pressure chambers the pressure usually varies from 760–1150 mm Hg; the air temperature from 22–25° C; the R.H. is usually constant at 50%; air movement 0.1–0.2 m/sec; number of complete air exchanges 10 times/h; air exchange/person 25 m³; wall radiation 0.6 cal/cm²/min; air colloid being freed from allergens. Usually there is no special ionisation. It takes roughly 30 minutes to reach maximum pressure, which continues for 30–45 minutes, and 30 minutes for the pressure to drop to that of sea level. Treatments may be daily. Patients are preliminarily given an aerosol treatment with spasmolytics and secretolytics (see p. 610).

(2) *Physiological effects.* According to Dirnagl and Stieve[3589], the following

physiological reactions are observed in a pneumatic chamber: Increased alveolar partial oxygen pressure; increased partial nitrogen pressure; decreased breathing frequency; increased depth of breathing; increased vital capacity; lowering of the diaphragm; compression of the intestinal gases; increased peripheral resistance; reduced pulse frequency and circulation of the blood; shift in mood to euphoria (*i.e.* pathological elevation of mood).

A surplus pressure of 2 atmospheres enables the body tissues to absorb 15 times more oxygen than usual (recent observations by Boerema). Whereas at 760 mm pressure the partial oxygen pressure in expired air amounts to 159 mm, in alveolar air 104 mm Hg, under 1150 mm Hg these oxygen values increase to 241.5 and 161 mm. Also the partial pressure of nitrogen increases. Experiments with helium, which keep the N_2 partial pressure at a constant level, have shown that the euphoristic mood, observed in divers in caissons and in patients in high-pressure tanks, is due to the increased nitrogen partial pressure which seems to affect the functioning of the rhinencephalon (see p. 302), a centre of the brain which plays such an important part in the mediation of the nature of moods.

(3) *Therapeutic effects.* Various successful treatments have been reported. Pulmonary emphysema (*i.e.* dilatation of air vesicles with loss of normal elasticity of lung substance), in particular functional emphysema as a result of spastic bronchitis and bronchial asthma, is favourably affected because of an increase in pulmonary ventilation and vital capacity, decrease in breathing frequency, greater elasticity of the diaphragm, increased oxygen saturation, etc. Chronic and subacute bronchitis, particularly the spastic type, is improved because of the increased pulmonary ventilation and greater facility of expectoration. Post-pleuritic residues and also atelectasis (*i.e.* non-expansion of the lungs, a major cause of anoxia and death) are successfully treated in these pneumatic chambers. Recent studies by Boerema (Professor of Surgery at the University of Amsterdam) have shown that hypothermia combined with high pressure greatly facilitates heart operations, during which the circulation of the blood through the heart has to be stopped for more than 10 minutes. It was also found that *gas gangrene* (a rapidly increasing necrotizing inflammation as a result of wounds or accidents, caused by anaerobic bacteria *Clostridium welchii*) and *gas phlegmone* (development of gases in muscular tissues of wounds due to the action of anaerobic bacteria, which develop CO_2 from carbohydrates and H_2S from proteins) are rapidly cured after a patient has been kept for 1 or 2 days in a pneumatic chamber of 2 atmospheres. This is due to the heavy saturation of the tissues with oxygen, which prevents the development of anaerobic bacteria.

(4) *Unfavourable effects.* They have been observed in all acute infectious diseases of the respiratory tract which are accompanied with fever; sinusitis; pertussis (whooping cough) and tuberculosis; various heart diseases (such as myocardial infarction, angina pectoris, etc.), serious metabolic disorders, hypertonia, and gastro-duodenal ulcers.

(5) *Methods used.* An excess pressure of only 240 mmHg is applied during the first two periods of treatment, followed by 20–30 treatments with 360–380 mmHg. Further treatments do not seem to have any additional effect. According to Baumann[3563] these treatments should be given daily in a continuous series.

(b) Low-pressure or high-altitude chamber

Low-pressure chambers for therapeutic purposes were used for the first time by Clanny in England[3576] and Junod in France[3600] around 1835. The foundations for modern low-pressure treatment were, however, laid by Bert in 1870. It is mainly due to the research carried out in the field of aviation medicine[3621] that the scientific basis was laid for the therapeutic use of low-pressure chambers.

As a result of these studies it was found that the influence of the reduced pressure as such is relatively small and the main therapeutic effect is due to the decreased partial oxygen pressure. For all that, the reduction in pressure itself has certain effects: it *decreases the pressure on lungs and arteries* and causes *changes in volume of gases enclosed in body cavities,* such as nasal cavities, dental roots, dental granuloma, gases in stomach and intestines, etc. The sudden lowering of pressures can be painful, particularly in cases of inflammation of dental roots, catarrhs of the middle ear tube, distension of stomach and intestinal gases, etc.

It was pointed out on p. 293 that an increase is also observed in *vital capacity, pulmonary ventilation* (at 3000 m altitude an increase of 13%, according to Cotes) and *evaporation* (according to Wagner an increase of 28–40% at altitudes of 2000–4000 m). The main stimulus, however, is created by insufficient oxygen saturation of the haemoglobin, which initiates a number of important regulating processes (see p. 294). The result of an oxygen stress treatment greatly depends on the speed at which the oxygen pressure is lowered and the minimum pressure is reached. Generally the raising speed is 1000 m in 1.5–2 minutes and the drop in elevation is 1000 m in 3–4 minutes. Because of the expansion of intestinal gases (almost twice the original volume at 4000 m), the intestines should preferably be emptied before the chamber treatment starts and the patient should be advised not to eat gas-producing food, *e.g.* various kinds of cabbages. Toothache during a chamber treatment usually indicates an inflammation of the dental roots.

The various pressure conditions and degree of oxygen saturation during low-pressure chamber treatment are summarized in Table 43. During a more prolonged stay at higher altitudes, gradual adaptation takes place. The period required for this adaptation greatly depends on the age (*i.e.* the reactivity) of the person. Studies on several thousands of visitors to spas at Bad Oberdorf and Bad Lippspringe (Germany) have shown that the acclimatisation period in days is approximately equal to the age in years divided by 5. However, this gradual acclimatisation does not occur in successive climatic chamber treatments; each treatment creates a new stimulus in the patient. This explains why initially favourable results observed at high altitude may disappear after the patient has remained for some time at this altitude. It is this difference in acclimatisation which has been successfully applied in low-pressure chamber treatments.

TABLE 43

PRESSURE CONDITIONS AND OXYGEN SATURATION DURING LOW-PRESSURE CHAMBER TREATMENT

Atmospheric pressure in the chamber	*Corresponding elevation*	*Oxygen partial pressure*		*Oxygen saturation of haemoglobin*
		in expired air	*in alveolar air*	
mm Hg	*m above sea level*	*mm Hg*	*mm Hg*	%
760	0	159	104	96
674	1000	142	86	94
596	2000	125	70	90
526	3000	110	58	85
462	4000	97	48	78
405	5000	85	40	70

The various physiological processes initiated as a result of oxygen stress have been discussed in detail on pp. 293–299.

The results of 25–50 climatic chamber treatments per day for four years at Bad Lippspringe, *i.e.* a total of roughly 40,000 treatments, have shown that the optimum elevation for most patients is about 2000 m (*i.e.* 596 mm Hg). Only in the case of whooping cough and training of the autonomic nervous system are greater heights recommended. The frequency and total number of treatments are as important as optimum pressure. The physician should resist the desire of many patients to be treated as often as possible and at a great elevation. Daily treatments may create psychic lability, disturbance of sleep and tiredness, even in healthy persons, as demonstrated by Dunker and Schwarz. The same physician or sister should, therefore, not accompany the patients daily in the chamber.

Armstrong[3560] tested healthy persons at 4600 m elevation, where they had to stay for 4 hours, but the best results were observed by Scholz von Mereny[3621], who treated his patients only twice a week for 1–2 hours at an elevation of 5000 m. After 8 treatments the height tolerance (*i.e.* the elevation at which unpleasant experiences may start) was increased by 1000–2000 m. In the experiments of Dunker, Schwarz and Armstrong this increase in tolerance was considerably less.

In Bad Lippspringe Nückel treats his patients in a chamber of $2 \times 3 \times 2.5$ m (comprising space for 6 adults) only twice a week for a period of 3/4–1 hour. Only children with whooping cough receive 3 treatments a week. After 8–10 treatments *i.e.*, 4–5 weeks) the treatment can usually be stopped. The experiments are carried out at a room temperature of 22–25° C, R.H. of 50% and air movement of 0.1–0.2 m/sec. The air exchange is 2500 l/min. and wall radiation amounts to 0.6 cal/cm²/min. The air is free from allergens.

3. *Methods of Treating Various Diseases*[3559–3631]

by

H. NÜCKEL

Indications for low-pressure chamber treatment

The experiences of the last four years at Bad Lippspringe based on about 40,000 chamber treatments suggest that the following diseases can be successfully treated in low-pressure chambers: spastic bronchitis (inflammation of bronchi) and bronchiolitis (inflammation of the bronchioles), bronchial asthma, the sinobronchial syndrome (*i.e.* chronic sinusitis accompanied by slime and purulent discharge), pneumoconiosis (*i.e.* lung fibrosis due to silicosis, siderosis, etc., see p. 113), pertussis (see p. 533), certain anaemic conditions, dysfunctions of the endocrinal and autonomic nervous systems.

Contra-indications for low-pressure chamber treatment

Low-pressure treatment should not be applied in the following circumstances: all conditions of oxygen deficiency of the heart muscle (myocardial infarction, angina pectoris, etc.); high degree of anaemia (haemoglobin values of 50%); lung tuberculosis (low-pressure treatment may activate dormant processes and may even cause haemorrhage from the lung); acute infections (accompanied by fever) of the respiratory tract and of the middle ear tube; acute rhino-pharyngitis; acute gastro-duodenal ulcers; colostomy (*i.e.* fistulization of the colon); laparotomy (*i.e.* incision in the abdominal wall); epilepsy; capillary fragility; high liquor pressure and recent lumbar puncture.

Examples of low-pressure treatment

In Nückel and Lincke's original publication, various low-pressure treatments were fully discussed. Only a few cases will be briefly reviewed in the present section.

Bronchial asthma, particularly in children and young adults, has been successfully treated by a 2000 m stress twice a week (with an interval of 2–3 days), each treatment lasting about 1 hour. The number of treatments required vary from 8–12 to 20–30. In cases of status asthmaticus, the hypoxia usually disappears after an hour at a pressure condition equal to 800–900 m and chamber temperatures of 22–25° C, R.H. of 40%. The treatment can be repeated on successive days because of the small oxygen stress involved. Gradually the intervals between the treatments and the elevation should be increased, the latter to 2000 m.

Pneumoconiosis has been considerably relieved by 2000 m treatments twice a week for a long period. The increased vital capacity and pulmonary ventilation, the reduction in breathing resistance and increased blood circulation in the peripheral arteries apparently reduce the fibroid degeneration in the lungs.

Pertussis. The successful low-pressure treatment of whooping cough was discussed on pp. 533–534. Contrary to the treatments described, a pressure reduction equal to 4000 m altitude is required. After this altitude is reached 3–5 times the altitude is changed from 4000 to 3500 m and *vice versa,* followed by a rather rapid rise (*i.e.* in 15 minutes) in pressure to sea level at the end of the one hour treatment. The treatment is repeated every other day. Total number of treatments about 4–6. During and after the treatment the chamber must be disinfected with U.V.-*C* light of 254 m μ wavelength and aerosan sprays.

Mild anaemic conditions are often considerably improved by a 4000 m treatment once a week for 3–4 weeks.

Endocrinal function. In view of the influence of oxygen stress on various endocrinal functions (see p. 294), it is not surprising to find that low-pressure treatment, in the case of endocrinal dysfunction, acts as a kind of shock treatment which often stabilizes the endocrinal functions. Treatments at 2000–4000 m altitude (often even less), 1–3 times a week (total number of treatments 6–12), in particular, have proved to be successful.

Autonomic nervous system. Considering the strong effect of oxygen stress on the autonomic nervous system (see pp. 293–294), the same successful treatments have been used for patients suffering from a dysfunction of the autonomic nervous system.

General convalescence after operations or serious diseases is considerably speeded up after low-pressure treatments (first 1000 m, gradually increasing to 2000 and 4000 m, twice a week, total number of treatments 4–10). The oxygen stress increases general metabolism and appetite and strengthens the nervous system.

Prophylaxis. Low-pressure treatments have also been recommended as a prophylactic treatment. The increased sensitivity of the nervous system (see p. 294), the stimulation of the circulation in peripheral arteries, increased 17-KS secretion, the increased capillary resistance and improved pulmonary ventilation increase the general and local resistance of the body to infectious diseases considerably. The treatment starts at 2000 m, 2–3 times a week; gradually the altitude is increased to 4000 m, the total number of treatments is 6–10. The treatment should be combined with U.V. treatment and massage.

Thyroid. Studies by Verzar *et al.* (see p. 273) suggest a decreased thyroid activity at 490 mm Hg (3450 m), not at 596 mm Hg (2000 m). The effect of low-pressure treatments of hyperthyroidism needs further investigation.

Polyarthritis. The beneficial effects of low-pressure treatments on certain forms of rheumatic disease, polyarthritis in particular, were discussed on p. 558.

Although a number of other diseases would in all probability respond well to this low-pressure treatment, considerable research is required to solve the many problems still facing the physician engaged in climatic chamber treatment.

Subsect. E. THALASSOTHERAPY

Thalassotherapy consists in utilising the beneficial effects of seawater and seaclimate upon the human body. In the present study we shall discuss only the climatological aspect. Although quite a few papers have been published on the subject, many are not based on critical physiological or clinical observations. Some of the interesting papers have been summarized in the refs.[3669–1062].

1. *Physiological Principles of Sea Climate Treatment*

For the characteristic features of sea climate see pp. 26 and 504. The most important meteorological factors of sea climate which may affect the physiological processes in man are:

(1) *Great air turbulence* due to usually strong winds along the coast, causing a considerable cooling of the human body.

(2) *Great intensity of the reflected solar energy,* which may be twice that from a field of grass in the case of water and four times in the case of sand. The effect of excessive heating of the skin by strong infra-red radiation is usually reduced by the cooling effect of the sea breeze.

(3) Daily and seasonal *differences in temperature* near the coast are smaller than inland (see p. 26). Winter temperatures are relatively high, summer temperatures relatively low; there are fewer frosty days.

(4) *Humidity* is greater near the coast, but owing to greater air turbulence, foggy conditions often tend to clear up more rapidly than inland.

(5) *Trace elements* of the atmosphere near the coast usually have a higher ozone content, particularly when there is a sea breeze (see p. 89); the iodine content is sometimes higher with tropical maritime air masses (see p. 97); the magnesium chloride content is usually higher near the coast, especially with strong onshore winds; the sodium chloride content is always high.

(6) *Air pollutants,* such as dust, pollen and chemicals, are usually rare as long as a strong sea breeze is blowing. This may change with a wind from the land.

(7) The *number and type of ions* are different near the coast. According to Schulz[3891a, p. 35], the number of large (Langevin)ions is greatest far from the sea, while the small ions are more abundant near the coast. Along the North Sea coast the percentage of small ions may be 40–45% of all ions, whereas inland only 6% is recorded. On the other hand, the total number of ions near the coast may be only 4500/cm^3 against 20,000 inland. Judging by the observations made by Krueger *et al.* (see pp. 353–362), these differences may have important biological effects.

In view of the climatic characteristics of coastal areas, certain patients should be advised not to live near the sea coast, whereas it may be beneficial to others.

(1) Owing to the greater *air turbulence and cooling* near the coast, patients suffering from diseases associated with a dysfunction of the thermoregulation mechanism, such as bronchial asthma and various rheumatic diseases, should preferably not undergo thalassotherapy. The cold stress, due to cooling air and, in particular, cold sea-water bathing, increases diuresis and 17-KS secretion. The latter factor may enhance the general resistance of the body to infections (see p. 516) but for patients suffering from kidney

diseases the increased diuresis may have unfavourable effects. It is evident that in warm countries with little air turbulence a sea climate may even benefit asthmatics and rheumatics.

Whereas these cooling effects are harmful to certain diseases, they invigorate the thermoregulation mechanism of healthy persons and strengthen their resistance to infectious diseases (see p. 516).

(2) Excessive *ultraviolet radiation* may be harmful to patients suffering from excessive secretion of gastric acid (see p. 343). On the other hand, it seems to stimulate the appetite of healthy persons spending a holiday near the coast; the time required for food to pass through the intestines appears to be shorter. According to Ellinger (see p. 567), in hyperthyroid persons exposure to ultraviolet may cause an exacerbation of their hyperthyroidism. The effect of excessive radiation along the coast on the pituitary was demonstrated in Jugoslavia by Milin (see p. 261). On the other hand the beneficial effect of ultraviolet radiation on bloodpressure, haemoglobin content, calcium and phosphate level of the serum and protein metabolism* (see p. 345), and its destructive effect on microorganisms (see p. 518) are favourable features for many patients living in a sunny sea climate.

Owing to these various climatic stress conditions, some people, especially those with a non-stable autonomic nervous system, may be thrown out of balance during the first week of their stay at a sea-side resort. Jungmann, Schultze, Trauner and others have evidence that two to three weeks are generally required at the coast for complete acclimatisation and that some patients (particularly children) may need as much as 5–6 weeks. This may explain why a short holiday at the coast can be detrimental, whereas an extended stay is decidedly curative in some cases. According to Häberlin[3891a, p. 94] it is also very important to consider the typology of the patient (see p. 672), because the same thalassotherapy may have opposite results in different human climatic types.

2. *Effect of Sea Climate on Diseases*

The application of climatothalassotherapy dates back to ancient Greek and Roman times. During the Middle Ages, and up to about 1700, however, thalassotherapy was practically unknown. It was mainly due to the English

* Studies by Häberlin and Müller[3891], Gauvain, Kleinschmidt[3938] and others suggest a 40–50% increase in basal metabolism in people visiting the coast for some weeks. According to Haeberlin, an increase in weight of 6.7% was observed in boys from 4–14 years after 6 week's treatment; in girls of the same age 7.2% (normal increase 1.05%). This increase took place without excessive accumulation of fat.

physician Russell (1700–1771) that the first extensive study was made of the therapeutic effect of sea water and sea climate. Lettsom and Latham continued his work during the late 18th century which led to the building of the first thalassotherapeutic sanatorium in 1796, in South-eastern England, *viz.* Margate. An interesting summary of the historic development of thalassotherapy in various W. European countries was given by Häberlin[3891a, pp. 45–52], one of the most prominent founders of thalassotherapy in Germany.

It is outside the scope of this book to review all the published observations concerning the effect of sea climate on diseases. Only the reported influence on a number of important diseases will be reviewed very briefly.

Respiratory diseases

It was pointed out on p. 504 that most physicians agree that lung tuberculosis and serious cases of chronic bronchitis should not be treated on the coast. Asthmatics (bronchial asthma) living near the coast in windy areas, with much fog and considerable daily fluctuations in environmental cooling, often improve considerably on moving a few miles inland. On the other hand, sea bathing on days when there is little or no wind is reported to have favourable effects because the sudden cold stress trains the thermoregulation system and stimulates the orthosympathetic nervous system. Also, if bronchial asthma is due to allergens, sea climate may be beneficial. The same applies to hay-fever and allergic rhinitis (see p. 462).

Chronic nose and throat catarrhs usually improve rapidly near the coast or during a sea voyage.

Owing to the greater cooling effects near the coast, the thermoregulation mechanism of a normal person is trained during thalassotherapy and this may be one of the reasons why people living near the sea suffer less from the common cold. According to Häberlin[3891a, p. 74] the lowering of the skin temperature due to cool air on the beach or after sea-bathing is greater at the end of a holiday at the sea coast, than at the beginning; but the rise in temperature after warming up in a room, is greater. In other words, during thalassotherapy the heat loss during cold stress becomes less and less and the patient becomes more resistant to cold stress.

It has also been suggested that the sodium chloride aerosol in the coastal air is a favourable factor. According to Gautier, the salt content is 5–22 mg/1000 l of air (total volume of air passing through the lungs in the course of a day being more than 20,000 l). Further study is required to analyze the influence of sea climate on the various factors affecting the "local resistance" of the body as explained on p. 511.

Skin diseases (see pp. 563–564)

Häberlin and Kalkoff (see p. 504) reported favourable effects of sea climate on skin tuberculosis (lupus vulgaris). Häberlin, Ménard, Calvé and others (see p. 505) are of the opinion that abdominal tuberculosis and osteotuberculosis can also be successfully treated at sea side sanatoria in W. Europe, particularly during the winter season.

Thalassotherapy improves the blood circulation in the skin and, therefore, its elasticity. After 6 weeks the red colouring of the skin after cold application is considerably more pronounced than shortly after arrival at the sea coast.

According to Döhring and Häberlin[3891a, p. 107], various forms of eczema (*e.g.* eczema pruriginosum), allergic dermatoses, neurodermatitis, psoriasis (see p. 564), furunculosis, etc. respond to thalassotherapy.

Diabetes (see p. 560)

Catrein[3745] observed in Warnemünde (Germany) an increase in the blood sugar level of 10–40% in healthy persons after a period of sea bathing. Therefore, most workers in the field of thalassotherapy do not advise diabetics to go in for cold sea bathing. On the other hand, wind-protected sun bathing usually lowers the blood sugar level.

Heart diseases (see pp. 505–510)

Considering the influence of strong cooling on various heart diseases, in general thalassotherapy cannot be recommended for heart patients unless the sea-water bathing takes place in swimming pools of warm sea water protected from the wind. However, as ultraviolet radiation often has a favourable effect on the blood pressure of hypertonics (studies by Loewy, Curschmann, Neefe and others), a holiday on the coast may, with due discretion, be of benefit even to heart patients, particularly if only psychological stress is the main cause of the heart trouble. A slow and gradual adaptation to cold, but brief, sea-water bathing may have a very stimulating effect under these specific conditions. Berg and Zeplin state that the blood pressure of hypertonics adapted to the cold can be seen to drop by 10–20 mm Hg in 20 minutes after a short spell (5–8 minutes) of sea bathing.

Blood diseases

Anaemia, which is characterized by a decrease in the erythrocyte and/or haemoglobin content of the blood, is often successfully treated at the sea coast according to Bracher[3728], Häberlin[3842, 3843], Wolff[4061], Scheel[4024] and others. Häberlin even reported an increase in haemoglobin from 30–70% in anaemic patients. The average number of erythrocytes may increase by half a million. Conradi[3750] says that an abnormal leucocyte level is also quickly restored as a rule. The blood sedimentation rates are reduced (according to Scheel[4024]). Successful treatment of anaemia is observed only in its temporary forms. In the case of pernicious anaemia, leucaemia, etc., a seaclimate apparently has an aggravating effect, according to Curschmann[3753] and others. This view is supported by various reports suggesting a higher incidence of these diseases near the coast.

Nervous and mental diseases

The majority of nervous patients should be advised to avoid a marine climate. In many instances a forest climate (see p. 679), may have a soothing effect on the patient.

Nicolas[3987], Leblanc[3961] and Curschmann[3771] noticed that patients suffering from migraine responded well to sea air.

Epileptics (see p. 539) and patients suffering from chorea infectiosa (*i.e.* St. Vitus' dance, a nervous disease with involuntary irregular movements) should not be advised to visit sea resorts because of the strong cooling effects and intensive sunlight which, on the other hand, have a favourable (*i.e.* quieting) effect on schizophrenics (see p. 536).

According to Curschmann[3771], Laignel-Lavestine[3955], Krauel[3950, 3951], nervous patients with an overstimulated parasympathetic nervous system are favourably affected by sea climate. Its influence on the mental efficiency of schoolchildren was briefly described on p. 675.

It is evident that part of the beneficial effects of sea climate is entirely due to psychological factors (lack of responsibilities, gaiety of beach life, etc.), but a number of direct meteorotropic influences on mental and nervous diseases cannot be denied. It is this observation which made Huntington[1753, 1755] believe that people living near the ocean are more productive and energetic than populations living in the centre of continents. This might also account for the desire of coastal nations all through history to explore new parts of the world.

Goitre

Thalassotherapy is a highly successful treatment for simple goitre, but we have it on the authority of Ellinger that hyperthyroidism is apt to be exacerbated by over-exposure to sunlight in cases of exophthalmic goitre.

This concludes our brief section on thalassotherapy, a field of study which is very old historically, but extremely young within the context of accurate scientific research. Many of the empirical rules given in this section are but partly understood and only future research may be able to develop thalassotherapy into a new powerful tool of therapeutic medicine.

Subsect. F. CLIMATIC HEALTH RESORTS (SPAS)[4063-4076]

1. *Introduction*

The previous chapters have clearly demonstrated the profound influence of weather and climate both on healthy man and the diseased person. As each climate has its specific meteorotropic effects, the obvious course is to study the possibility of selecting certain areas with very specific climatic conditions as the location for the treatment of certain diseases. Such areas are known as *climatic health resorts,* also known as *Kurort* (in the German-speaking countries) or *spa* (in the English-speaking countries). In the following sections only the word "spa" will be used.

The therapeutic effect of each spa can be classified into three groups of factors:

(1) Influence of *hydrological* treatment, also known as *balneological* treatment. This consists of two different treatments: (*i*) Influence of baths in thermal waters, *i.e. external balneological* treatment. This latter treatment, which consists of a thermal, a physico-chemical and a hydrostatic stress on the skin, is often combined with massage, aerosol inhalation, etc. Also, mud-baths are used instead of water. (*ii*) Drinking thermal waters, *i.e. internal balneological* treatment.

(2) Influence of the *local spa climate,* also known as *balneo-climatotherapeutic* treatment.

(3) Influence of *psychological* factors. The influence of this factor, which comprises the effect of a holiday without any responsibilities, the healthy life (the patient goes to bed very early and wakes up rather late, in the afternoons he takes another nap), the gaiety of many spas with concerts and so forth, is so important that without considerable research it is impossible to determine whether an observed improvement is really due to the actual balneological treatment, either hydrological or meteorological or both.

Despite the purely empirical and rather unscientific approach of most spas, the interest of the general population and physicians in spa-treatment is enormous, particularly in countries like Belgium, France, Germany, Austria, Switzerland, Italy, Poland, Czechoslovakia, Jugoslavia, Roumania and the USSR. It is all the more regrettable, therefore, that, notwithstanding the considerable funds which are available in these large spas, little or no interest exists in scientific research, in which, for example, two groups of people (similar in age, sex and profession) are compared, both groups living under practically the same holiday conditions, but one taking balneological treatment, the other group not.

From a practical point of view it may be indifferent to the spa administration whether a successful treatment is due to psychological or balneological factors. However, it is not sufficiently realized that only as a result of systematic research may it be possible to include balneological treatments in the officially recognized scientific medical treatments; and an even more important point is that, as a result of such research studies, it may be possible to develop scientific balneological treatments which may ultimately be more conducive to the improvement of the patient than the methods used so far.

In the following sections we shall discuss a number of rather well-established observations which seem to warrant further research in the field of balneotherapy. Scientific research probably will discover a number of important physiological effects of balneological treatment which will support, perhaps not all,but at least a great part of the empirically discovered results of balneological treatments. The following two subjects will be briefly discussed: the physiological principles involved in balneotherapy, and the effect of balneo-climatic treatment on various diseases.

2. *Physiological Principles involved in Balneotherapy*

A patient visiting a spa for a short period is only subjected to the daily changes in the local weather conditions, but if he stays for a considerable time, an important factor is the average daily meteorological conditions, *i.e.*, the local microclimate of the spa. The daily weather and microclimatic conditions of a spa are closely related to its general location. In mountainous areas the general weather conditions and the biological effects of a *mountain climate* (see pp. 27 and 293–299) will prevail, near the coast that of a *sea climate* (see p. 643); inland it may be a *forest climate* (see p. 679) and so forth. The characteristics of different regional climatic zones were enumerated on pp. 27–28 and the meteorotropic effects of each of these climates were fully discussed in previous sections. As practically all the climatic zones can be found in many large countries, a scientific study of the biometeorological characteristics of the various spas in such a country would enable a physician to find a favourable one for almost every meteorotropic disease.

As indicated above, balneotherapy is a complex mixture of hydrological, climatic and psychological treatments. The physiological principles involved in various climato-therapies have been reviewed in previous sections, in particular in the preceding section on thalassotherapy. For this reason only a brief review will be given of the physiological principles involved in hydrological treatment as such.

Influence of external balneological treatment

(1) *Influence of thermal stress.* (*i*) It has been pointed out (see p. 330) that, according to Zimmerman and others, an *increased 17-KS secretion* can be observed after warm thermal baths and after sauna baths. (*ii*) The effect of considerable *heat stress in thermal baths* on oxygen exchange, general circulation, cardiac output, blood pressure, pulse rate, peripheral resistance, dehydration, etc., as studied by Bazett, Scott, Maxfield and Blithe, were discussed on p. 248. The effects of such a thermal bath treatment will depend on the hour of the day (*i.e.* the biological rhythm, see pp. 200–201), sex and age of the patient (see p. 229), his personality pattern (see p. 229), the season (see p. 575) and the degree of acclimatization (see p. 242).

(2) *Influence of physico-chemical stress.* (*i*) Experiments by Buettner and others (see p. 218) have shown that the outer horny layer of the skin, the stratum corneum, *is not as impermeable as one may be inclined to believe.* Experiments in heavy water have shown that a foot or arm placed for one hour in 100 cm^3 water may absorb 2 cm^3. A small portion remains in the epidermis but the major part enters the system and is finally excreted in the urine. It is not only water, but also water vapour that can penetrate the skin. The water and vapour intake increases with increased temperature and activity of the body. A high concentration of salt, exceeding 5% NaCl, causes a decreased water uptake with increased salinity. With 10–15% NaCl, the transfer ceases. Stronger solutions draw water out of the skin*. Due to the fluid penetration into the skin also some of the trace elements will penetrate into the body and this explains the dangerous effects of certain hormone products sold as bathing salts and sometimes used by women in the menopause to rejuvinate their skin. Particularly chemical compounds which have a dissolvent effect on fatty substances of the skin can penetrate

* In normal sea water the total salt content is about 33-37 g/l (33 in northern polar seas, 34 in the Antarctic, 36 in the tropical Pacific and Indian Ocean, 37 in the tropical Atlantic Ocean). The various salt percentages are the following: NaCl 78%, $MgCl_2$ 11%, $MgSO_4$ 4.7%, $CaSO_4$ 3.6%, K_2SO_4 2.6%, $CaCO_3$ 0.34%, $MgBr_2$ 0.22%.

A thermal spring, for example, in the well-known Kurort Baden (Switzerland), produces 4.5 g of salts/l, at a temperature of 48° C, comprising about 2 g NaCl, apart from many other salts of calcium, magnesium, potassium, lithium, strontium, etc. In German law, only springs with more than 1 g of salts/l of water or temperatures above 20° C can legitimately be called "curative springs" (Heilquellen). Other curative springs should be called "mineral springs".

more easily. According to various authors[1072] particularly CO_2, H_2S, arsenic acid (H_3AsO_4), thiosulphuric acid ($H_2S_2O_3$), chlorides, bicarbonates and various salts of heavy metals (such as iron, copper, cobalt, manganese) belong to this group of compounds. (*ii*) On p. 610 it was pointed out that an iso-osmotic pressure of tissue fluids requires 0.9% NaCl, 1.8% Na_2SO_4 and 3.4% $MgSO_4$. A hypertonic thermal water will cause a *shrinkage of the body cells* by dehydrating the cells. (*iii*) According to Terrier thermal water containing 0.45–0.48 cm³ H_2S/l would cause a penetration of *sulphur* into the blood circulation. As indicated on p. 263, according to Goldzieher there seems to be a close relationship between adrenal cortex, liver function and sulphur metabolism. This could be one of the reasons of the supposedly favourable effects of thermal sulphur springs on certain rheumatic diseases. A similar explanation has been given for the favourable effects of lithium waters which would assist in dissolving uric acid compounds (see p. 546, podagra). (*iv*) The penetration of thermal water through the skin will affect also the *diuresis* and *functions of the kidney*. (*v*) Most likely the penetration of solutions through the skin affects also the *peripheral nervous system*, but no accurate data are available. This stimulating effect has been attributed to ionic reactions in the skin as a result of the acidity of the skin (pH about 3.7). The free hydrogen ions are replaced by various cations, such as K, Na, Ca, Mg, Al, Mn, Zn, Cr, Fe (in this order of intensity), particularly in warm solutions. (*vi*) Thermal water will also affect the *acidity of the skin*. As explained on p. 511, the acid coating of the skin plays an important part in the local resistance of the body to infectious diseases in general and skin diseases in particular.

(3) *Influence of hydrostatic stress*. It has been suggested that the hydrostatic pressure in a bath may also have important physiological effects. The circumference of the abdomen during thermal baths may be reduced by 3–6 cm. The pressure on the extremities affects the blood flow and function of the heart.

The problem of the reduced weight of a body floating in water has been studied notably in space medicine (see p. 715). The floating condition is described as *hypodynamic environment*, the study of the physiological changes during prolonged immersion of a body as a result of weightlessness is called *hypodynamics*. The following observations were made[4063a, 4069a,b]: (*i*) The immersion of a body in water for a week, except for one hour a day outside the water tank, the subject being clothed in heavy cotton underwear and a skin-tight rubber suit, caused a reduction in the total amount of sleep, constriction in the range of sleep states and progressive improvement of the stability of the sleep states. There were no signs of sleep deprivation despite the reduction in sleep. This was explained by McKenzie *et al.* as a reduction in neuro-muscular effort and energy expenditure during this weightless state. (*ii*) As early as 50 hours after immersion a change in psychomotor efficiency was observed. After a seven-day immersion period the response time during various experiments was considerably increased. (*iii*) After a prolonged immersion Graveline and Balke observed a severe disturbance of cardiovascular reflexes (for example decreased cardiorespiratory adaptability) and diminished muscular tone. An increase in the white blood cell count, total urinary nitrogen and haematocrit content has also been reported.

Influence of internal balneological treatment

Although this non-meteorological aspect is outside the scope of the present book, a few words should be said on the subject because this internal hydrological treatment may considerably affect the climatological results. The drinking of thermal waters may admit two kinds of substances to the stomach, *viz.*, fluids and gases.

(1) *Gases.* An important gas is *radon* (see p. 87) which is present in the atmosphere in very small quantities but which may occur in considerable quantities in certain thermal springs. The drinking of such water or inhalation of aerosols prepared with this water is known as *radon therapy, emanotherapy* or *radium emanation therapy.* The aerosols usually contain less than 80 Mache units (M.U.)/l of air, the fluids 800 M.U./l. Engelmann who studied the matter in 1920 at the Physiological Institute of the University of Frankfurt, suggests that the radon radiation stimulates cell functioning and, in particular, the oxidizing processes. Thermal waters rich in carbon dioxide (*i.e.* at least 1000 mg CO_2/l water) apparently stimulate gastric secretion and the digestion of food.

(2) *Fluids.* The fluids which are drunk are usually complex mixtures of various salts. Both the chemical composition and pH of these fluids may affect the stomach and intestines considerably. (*i*) For example, *alkaline waters* (preferably taken before meals) seem to bring alleviation to ulcer patients suffering from excessive secretion of gastric acid. They should not, however, be taken regularly by healthy persons. Changes in alkalinity of the stomach also affect the blood serum (see p. 292) and diabetics, *e.g.*, have sometimes, therefore, been advised to take alkaline waters (see p. 283, 286, 560). (*ii*) *Acid waters* (usually rich in HCO_3 and calcium) appear to increase the calcium content of the blood of people with a low calcium level. It does not affect a healthy person. Thermal waters rich in Na_2SO_4 and $MgCl_2$ (or $MgSO_4$) cause accelerated digestion; $MgCl_2$ waters stimulate bile secretion

by the liver and assist relaxation of Oddi's sphincter (see p. 289) and the tonic contraction of the gall bladder. We have seen on p. 289 that bile salts facilitate the digestive action of all pancreatic enzymes; they promote the absorption of the vitamin's D and K and the physiological processes affected by these vitamins (see p. 584). (*iii*) *Arsenic waters* (*i.e.* waters containing more than 1 mg arsenic/l, the toxic dose being 10 mg arsenic) have been recommended because arsenic tends to reduce the activity of the thyroid in cases of hyperthyroidism; it has a regulating effect on the cornification of skin and nails; it seems to stimulate the formation of erythrocytes and reduces the formation of leucocytes (according to D'Haenens, arsenic accumulates more especially in the spleen, see p. 283). It has therefore been recommended for leucaemia patients and for cases of secondary and pernicious anaemia. Good results have also been reported with psoriasis and chronic eczema. However, as the regular consumption of even small quantities of arsenic may induce cancer, a continuous course of arsenic waters should not be lightly recommended. (*iv*) *Sulphur waters* (containing more than 1 mg of sulphur, usually as H_2S) have been recommended for rheumatic diseases, itching skin diseases, etc.

In a word, there seems to be little doubt that balneological treatment may bring about objective physiological changes in the human body, whether favourable or unfavourable; but, owing to the psychological factors involved in such a treatment and the lack of systematic research up to date, it has not been possible to determine the exact physiological processes involved in hydrological treatment.

3. *Effect of Balneo-climatic Treatment on Various Diseases*

A number of successful balneo-climatic treatments of various diseases have been discussed in the previous pages, but it would go beyond our purpose to discuss this aspect in greater detail. A few general remarks will suffice.

Rheumatic diseases. A summary of the best climatic treatments and the precautionary measures to be taken appears on p. 558. It is there stated that warm thermal baths, mud-baths or sand-baths, surrounding the body and protecting it from local differences in infra-red radiations of the environment, act as a corrective to a disturbed thermoregulation mechanism. The taking of alkaline waters, which neutralize uric acid in the body, has proved to be beneficial for certain forms of rheumatism. Sulphur waters seem to stimulate the adrenal cortex and are therefore recommended for the treatment of various rheumatic diseases.

Diabetes. During periods of acidosis the drinking of alkaline waters is apparently very helpful and the patients seem to require less insulin to control their metabolism.

Skin diseases. We have seen that various skin diseases (*e.g.* eczemas, psoriasis, etc.) can be alleviated by balneological treatment.

Hyperthyroidism. Arsenic waters have been recommended for reducing thyroid activity.

Hypertension. Thermal baths have proved in many instances to reduce the diastolic blood pressure of temporary cases of hypertension.

It should, however, be realized that only a few of the reports are based on a large number of well-established statistical observations. Extensive research is therefore required before any of the statements above can be accepted as scientific facts.

CHAPTER 3

The Effect of Town-planning and Architectural Design and Construction on the Microclimatic Environment of Man (An Introduction to Urban Biometeorology)

by

J. K. PAGE

Section 1. Introduction

The majority of people in the world spend at least half their lives in the artificial climates which exist within the walls of buildings. Man's health is determined therefore just as much by the indoor climate of his home and workplace as it is by the outdoor climate.

The field covered by urban biometeorology is so large that it is only possible to consider broad principles. The subject falls naturally into two parts, the meso-climatology of the town considered as a whole unit, and the micro-climatology of the individual building and the space round about it. Section 3 of this chapter deals with the town planning aspects of the subject, and Section 4 with the problem of the climate in particular buildings. Section 5 considers briefly some climatological factors to be considered in the location, design and construction of hospitals and sanatoria. These three sections are preceded by a few paragraphs on the general methodology of urban biometeorology, emphasis being laid on medical considerations.

Section 2. General Methodology

In building one is concerned with an engineered climate. While doctors give a natural priority to hygiene, this is not so of the majority of people. There is always a tendency to put fashion and social status before comfort, and comfort before health, in practice, if not in theory. Comfort by reducing stress will normally contribute to health. Comfort however is sometimes achieved by accepting an even greater alternative stress, or even taking a positive risk to health, *e.g.* sitting over a coal brazier with an inadequate flue, a practice that kills quite a number of people every year.

The legislative approach to hygiene is sometimes adopted. It is not always very successful, and evasion may be widespread. For strict enforcement an army of health inspectors is required, and they are seldom available. For example, permanent ventilation is required by law in certain countries. If there is a cold season, one can be practically certain that a large proportion of such ventilators will be permanently blocked by the occupants. The fact is such ventilators make the room cold and less comfortable. Comfort is preferred to health. A far better way of handling hygienic matters is to try to get the hygienic practice the most comfortable one, and then there is unlikely to be any need for outside enforcement. In some upland areas of the tropics, for example, there is a lot of carbon monoxide poisoning from braziers[4101]. There are two solutions possible, either to insist on more permanent ventilation, or to insist on a proper flue. Given a proper flue, the relief from smoke and fumes is so great that no one would go back to burning a brazier without a flue. Hence one legislates, if possible, for the flue, and not for the ventilators, which will be sealed.

An ecological approach to environment is essential, because the interactions of environment with the human organism are so complex. One must consider all the human sense organs simultaneously, the thermal and moisture balance of the body and the chemical stability of a multitude of human tissues. For example, restricting natural ventilation in cold weather may reduce thermal stress by making the interior warmer. It may also increase physiological stress in other directions due to the increase in concentration of bacteria, the increase in concentration of tobacco smoke and other natural indoor pollutants and so on. The indoor humidity may rise to excessively high levels, and condensation may result. Evaporation rates may also be affected. Subtle balance has to be found between heat and moisture losses.

The poorer the community, the more difficult it is to find the correct balance between the demands of health and comfort. In N. Nigeria, for example, a well defined meningitis season appears in the cold weather. This is largely associated with the overcrowding which occurs in winter when people huddle together to keep warm at night. The traditional remedy for such epidemics is to construct small individual huts and sleep in them until the epidemic passes. This step however decreases comfort and is used only as a curative measure not as a preventive measure. In many modern tropical towns, particularly in plateau areas, tuberulosis is rife. Overcrowding and poor nourishment are to blame. Authorities often try to reduce the spread of the disease by legislation directed either at the number of people per room, or the amount of permanent ventilation. As the inhabitants' primary preoccupation is thermal stress due to cold, measures likely to make them colder are not very acceptable. Far saner are regulations likely to make them warmer. An extensive study has been made of this problem in S. Africa which showed that in upland climates heavyweight houses which store the heat of the sun against the night are much better than lightweight houses which are liable to be too hot by day and too cold by night, and standards were set accordingly[4098].

The variation of the quality of the "total" environment with season also requires consideration. It is sometimes possible to find design solutions which are suitable in one season and quite insupportable at another. The failure of many modern buildings to give relief from sun and heat during the hot summer provides a good example of the dangers of one season type of thinking, which so often prevails in architectural circles at the present moment. Traditional buildings often provide a more suitable biometeorological environment than the more modern styles that have replaced them; unfortunately few contemporary architects and engineers have adequate training in biometeorological principles. The consequent defects in their buildings are very obvious to the trained observer. Informed criticism from the medical profession should gradually help clear up some of these present shortcomings.

Finally a few words on synoptic biometeorology would not seem out of place. Many studies have been made on the relationship between weather and disease, but few of them have concentrated on the indoor climate. Correlations are usually based on standard meteorological data, which are only distantly related to the environment actually occupied by man, particularly in winter. Suppose it were agreed for a moment that the rate of ventilation of an office affected the general respiratory infection rate (a hypothesis subject to certain doubt as a result of certain recent experiments). The natural ventilation rate would be higher in cyclonic than in anticyclonic weather as the outside wind speeds would be on average higher. Hence one would expect to find a correlation between pressure and respiratory infection. It is easy to jump to the false conclusion that respiratory infection is influenced by changes of atmospheric pressure directly. This hypothetical example shows how important it is to try to get at the primary physical factors causing a condition. There are grave limitations in working solely with outdoor meteorological material and some attempt should always be made to understand what the outdoor data imply in terms of typical indoor environments. If the mechanism of causation can be elucidated, positive action can be taken to modify the indoor climates accordingly. Pathological biometeorologists could well give more attention to recent studies in architectural physics when considering the relation of particular diseases to weather.

Section 3. Influence of Town and Country Planning on the Climate and Health of Man

1. The Climate of Towns

The majority of meteorological stations are not located in the centre of towns. They tend to be on the periphery, often on a nearby airfield. The climate recorded at these stations may be very different from the climate of the centre of the town.[1096, 1093] A further complication is that the climate of the centre will change as further development takes place.

There are two basic ways of exploring the urban climate, either to set up a close network of stations on suitably selected sites[1083], or to use a mobile traverse technique linked with suitable base stations[1100]. The motor car has been widely used.

2. Temperature of Towns

The temperature regime in the centre of the towns is different from that of the surrounding country for four principle reasons: (*i*) There is an appreciable amount of generation of heat from stoves, fires etc., and machinery, particularly in winter. (*ii*) The thermal capacity of the buildings is high. This means the town centre heats and cools more slowly than the surrounding countryside. The heat of day tends to be stored in the masonry and then released in the evening. (*iii*) The absence of grass and vegetative cover except in parks and other open spaces reduces cooling by evapotranspiration. (*iv*) The presence of smoke pollution tends to cut down the incoming short wave radiation intensities. This is offset by the lower net rate of exchange of long wave radiation. Radiation losses to the sky at night are not so rapid as a rule as in the surrounding countryside.

The significance of these factors depends on the size of the town, as the recent study by Duckworth and Sandberg shows[1089]. The values given in Table 44 refer to the evening period, the time of greatest temperature differential. As is well known, the centres of cities tend to be particularly unpleasant during the early evening during heat waves. The same factors that tend to make the town warmer during the evening tend to make it cooler than the surrounding countryside during the early part of the day. The heavy masonry only heats slowly. Town climates are therefore much

TABLE 44

HORIZONTAL TEMPERATURE PATTERN CHARACTERISTICS OF THREE AMERICAN CITIES
(after Duckworth and Sandberg)

	San Francisco	*San Jose*	*Palo Alto*
Population	784,000	101,000	33,000
Incorporated land area, miles²	45.1	14.8	8.6
Population density, persons/miles²	17,383	6,824	3,837
Representative urban differential between city centre and countryside during (20–24 h)*, °F	10–12	7–9	4–6
Representative size of area at least 4° F hotter than surrounding countryside, miles²	4.0–6.0	1.5–2.0	0.1–0.3
Maximal observed urban differential between city centre and countryside, °F	20	14	13

* Time of maximum difference.

more pleasant in the morning in summer than in the afternoon and evening when the advantages lie with the countryside. The temperature regime of a town can be mitigated by providing suitable parks and open spaces (provided there is sufficient water available to support vegetation). Not only do these spaces produce a direct cooling effect by evapotranspiration, but they provide a "bolt hole" where people may relax during the heat of the early evening.

3. Wind Circulation in Towns

The circulation of the free wind in towns is much impeded by the presence of buildings. In London, for example, it was found that the wind speed at street level was on average one third of that on a site of normal exposure[4085]. The shielding effects of buildings are very considerable. The wind shadows may extend 10–15 times the height of the building in a horizontal direction[4090]. The resulting low air movements in towns tend to make conditions particularly intolerable in hot humid weather. It is advantageous however in winter to have low air movements, for the chilling effect of the wind becomes much less. Parks and open spaces once again provide areas of special amenity for summer on the grounds of greater wind circulation which takes place in them.

4. Sunshine in Towns

Pollution of the atmosphere reduces the sunshine in towns appreciably, especially in winter. For example, the sunshine recorded at Kingsway in the centre of London may be compared with the sunshine at Kew in the outer suburbs of London. Neither atmosphere is very clean, but the sunshine recorded in January at Kingsway was only 70% of that at Kew for the years 1952–'58, while in June the corresponding figure was 91%. The pollution is of course reflected in the lower radiation and illumination intensities recorded at the centre of cities. As is well known, the ultraviolet intensity may be very low in the centre of cities especially in winter. This was thought to have considerable biological significance in the 1920's and 1930's. The improved diet of the present day town dweller and the availability of supplementary vitamins make it a little dubious as to whether ultraviolet light is any longer of any great importance. Atmospheric pollution, as such, is probably the greatest urban menace to health today.

5. *Atmospheric Pollution* (see also pp. 106–148)

There are three general sources of pollutants in towns: smoke from domestic fires, from industry, and exhaust fumes from vehicles. Pollution from domestic premises, particularly if open fires are used, often presents a much more serious problem than is usually realized. The chimneys are low, often wrongly placed, and function badly and a great deal of the smoke reaches ground level. The rather higher chimneys used by industry function as a rule somewhat more efficiently, though excessive quantities of smoke may still reach the ground. The pollution may be divided into suspended solids and gaseous pollutants. Smoke and other solid suspended matter may cause inflammation of the respiratory tract. Even if this is filtered out, inflammation may still result from the acid gases, etc. These may have to be removed chemically.

The principle of zoning industry to reduce domestic pollution is often followed in town planning practice, but the greater use of electric power has lead to industry becoming a much less important source of pollution except in the case of certain dirty industries like iron and steel manufacture, chemical manufacture, smelting and so on. The danger of severe concentrations of acid gases being built up are greatest in anticyclonic weather in winter when inversions are particularly likely to occur, when the smoke becomes trapped below the inversion layer. The correct location of dirty industry, therefore, is not simply a matter of examining prevailing wind directions. As the most catastrophic conditions will usually occur under winter anticyclonic conditions, it is desirable to consider the direction of the prevailing winds during inversions as well as the general prevailing wind directions. The latter will affect the mean levels of pollution throughout the year. Both are important.

Several investigations have shown the value of parks and open spaces for reducing pollution. The vegetation used must be able however to withstand the degree of pollution present.

The problem of pollution from the motor car (see p. 96) is still unsolved, though various investigators are working on achieving more complete combustion of the various primary and secondary products by treating the primary exhaust. The dust, dirt, fumes etc. from congested urban roads undoubtedly do not contribute to health.

Section 4. The Influence of Architectural Design and Construction on the Microclimate in Buildings, with Special Reference to Human Comfort and Health

1. *The Climate inside Buildings*

Despite many similarities (see pp 82–86), on the whole the climate inside buildings is different from that prevailing outside, even in the case of buildings in which no mechanical equipment is provided to modify the environment. Priority in design tends to be given to the thermal environment; other environmental factors like daylighting, ventilation and air movement also require proper consideration.

2. *Thermal Conditions in Buildings*

Cold weather

In cold weather, comfort in buildings can only be achieved by using artificial sources of heat to raise the temperature. The size of the artificial heat source required may be reduced by increasing the thermal insulation. A balance has to be found in design between the amount of insulation provided and its cost. The colder the climate the greater the amount of insulation justified. One is not of course merely concerned with air temperature but with other factors that affect thermal comfort like the radiant environment and the rate of air movement[1084]. The cold exterior walls of poorly insulated buildings act as radiation sinks, and higher air temperatures are required for comfort than is the case in well insulated buildings with warmer walls. The rate of heat transfer from the body depends on the rate of air movement around it. One of the objectives in good design is to avoid rapid movements of air over the body which will be felt as cold draughts. The legs, in particular, are very sensitive to small air movements. If on the other hand the rate of air movement is too low, the environment may become rather lifeless. One attempts therefore to have a limited amount of air movement to make the environment more stimulating.

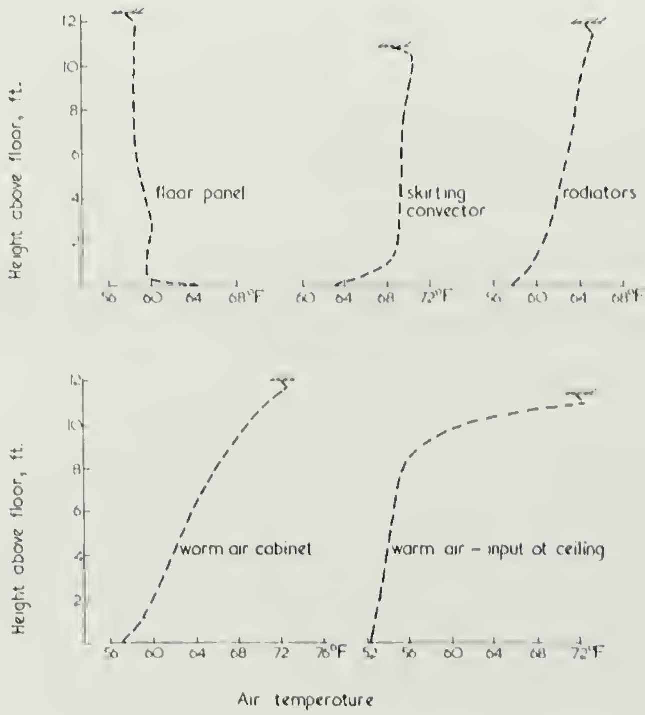

Fig. 97.

Temperature variation (vertically) in single storey schools. The interiors of buildings should not be thought of as constant temperature enclosures as measurements of vertical temperature gradients made in schools by the Building Research Station clearly show. Observe the influence of the type of heating used. Note air heating in particular; it tends to produce large temperature gradients due to the stratification resulting from density differences. (U.K. Crown Copyright reserved.)

The interiors of buildings should not be looked on as constant temperature enclosures. Fig. 97 shows typical thermal gradients with different types of heating system. Hot air systems, in particular, tend to give big vertical temperature gradients, especially if the discharge outlet is placed high in the room[4088]. The consequent conditions of hot heads and cold feet give an unpleasantly stuffy environment.

Floor heating by electricity or by embedded hot water pipes can be very effective provided care is taken to ensure that the temperature of the floor does not exceed about 80° F (27° C). Radiant panels embedded in the walls and ceiling are also satisfactory but may give rise to unpleasant physiological effects, if the radiation on the head is excessive. In this case panel size is important, the larger panels producing greater radiation gains than small ones.

The thermal capacity of the building is also important, particularly when intermittent heating is used. Lightweight structures cool rapidly. Heavier buildings can store their heat longer. In domestic practice, they tend therefore to be warmer at night particularly if the basic standards of heating are not high[4091].

Hot weather

Cooling buildings is a much more expensive process than heating them, and it is unusual for much mechanical equipment to be available for cooling except in very prosperous countries. A suitable environment has to be achieved instead by correct architectural design[4099]. It is necessary to start by considering what is the primary cause of thermal stress in a particular environment. A useful distinction can be made between hot humid environments where the basic physiological problem is the evaporation of moisture from the body and hot dry environments where the basic physiological problem is to reduce the rate of transfer of heat to the body. In desert climates, in particular, the air temperature may be appreciably above skin temperature in the middle of the day, and increasing the rate of air movement will only make conditions even more severe. The only remedy is to try to reduce the air temperature[4081]. This may be done in two ways; firstly advantage may be taken of the flywheel effect of heavy construction to damp out the midday peak. Secondly considerable cooling can be achieved by evaporation of water. Traditional construction in hot dry areas often makes use of devices like the "kus tatti" over windows. This type of device made from straw is soaked with water and provides cooling by evaporation. In humid environments the basic problem is to increase the evaporation of moisture from the skin[1094]. This means special attention must be paid to natural ventilation by wind forces. Mechanical fans can also help. The wind tends to drop at night in hot humid weather and conditions are likely to become particularly sultry during the late evening. It is advantageous in climates where hot humid conditions predominate, to use buildings of lightweight construction, for these cool rapidly, giving lower air temperatures at the time of greatest stress[4082].

Air conditioning

The object of air conditioning is to make the air inside more suitable for the purpose for which the interior is to be used. Full airconditioning implies full control of the temperature of the air, its moisture content, filtration of suspended particles and sometimes covers chemical washing to remove gaseous contaminants. Many air conditioning systems only allow for heating the air, increasing its humidity, and filtration of suspended solids, no cooling plant being installed for summer cooling or dehumidification.

In some buildings there is no recirculation of air, the conditioned air being exhausted directly to the exterior and being entirely replaced by fresh air from outside. This is expensive, and it is more normal to recirculate a large proportion of the conditioned air, making up say 1/5th with fresh air.

Two important physiological problems arise with air conditioning. One is the circulation of bacteria and other internal atmospheric pollutants like tobacco smoke from room to room down the ducts. This may, for example, present problems of cross infection in hospital practice, particularly if recirculated air is used. The other is the problem of duct noise. In badly designed systems, noise may pass from room to room, or along from the plant. This may be extremely disturbing to the occupants. Extreme economy in air conditioning is only likely to be achieved at the expense of efficiency. When air conditioning is used in medical practice, it is important to realize that ordinary filtration will only remove solid suspended matter. Gaseous pollutants like sulphuric dioxide can cause considerable bronchial irritation; therefore in the treatment of smog patients, chemical purification may be essential, especially in highly polluted regions. Simple washing is often beneficial, but this increases the relative humidity which is not always desirable.

The humidity in buildings

The relative humidity in heated buildings is normally lower than that outside, but the absolute humidity is usually higher. The decrease in relative humidity which results from the raised internal temperature, is offset to some extent by the moisture produced internally by the occupants themselves and by their activities like cooking, bathing, washing, etc. If the absolute humidity indoors becomes too high, severe condensation is likely to take place, particularly on the colder surfaces of the room. Such condensation often may be reduced by increasing the ventilation rate. Very low relative humidities which tend to occur in heated buildings with polar air masses in winter are undesirable indoors. They may cause an unpleasant dryness of the throat and possibly contribute to infection by producing an adverse moisture balance of the respiratory system. Very high humidities are liable to lead to dampness of clothes, etc, fungal attacks on walls and so on. It is normal in good building practice to aim to get the relative humidity in the broad region of 50%.

In summer the absolute humidities indoors are usually only slightly greater than more outdoors, as considerably higher ventilation rates than in winter are usual. The important exceptions are air conditioned buildings in which the air is dehumidified to increase thermal comfort. For example, considerable dehumidification is usually necessary for comfort in hot humid climates where the outdoor vapour pressure may exceed 35 mb.[1085].

Wind, natural ventilation, and air movement

Natural ventilation is the replacement of the air inside a building with fresh air from outside by natural forces. There are two mechanisms involved, forces set up by the natural wind, and forces set up by differences in density between the inside and outside air, the latter being known as the stack effect[1087]. If the wind is above about 3.5 miles/h, wind forces dominate. The greater the wind velocity, the greater the natural ventilation rate.

The desirable minimum ventilation rate is set by the need to avoid the excessive accumulation of body odours, and tobacco smoke, and to secure a favourable internal moisture balance. Excessive ventilation rates make it difficult to keep the interior warm, while low ventilation rates produce a stale unpleasant and often humid environment.

The actual natural ventilation rates achieved depend as much on the way the occupants use their windows as they do on the outdoor wind speed. Practice varies from country to country and from individual to individual.

Hygienists for a long time have stressed the importance of good natural ventilation on grounds of cross infection. The experimental evidence is however very conflicting on this point[1080]. Perhaps insufficient attention has been given to the detailed mechanism of transfer of infecting organisms. The evidence from some recent investigations in English hospitals indicates that distance between beds is more important than ventilation rates, and that dust, particularly from blankets, plays an important role. High ventilation rates during and after bed making are recommended to disperse the dust generated.

In hot weather comfort will depend very often on good air movement and windows should be suitably placed to provide it. Window design for hot humid climates has been extensively explored by wind tunnel studies[1092] in Texas. The window tends to act as a baffle. If correctly designed, it can direct the air where it is wanted, *e.g.* over the bodies of the occupants. Incorrectly designed, it may deflect the air stream towards the ceiling and other uninhabited parts of the room where it is of no benefit. It is probably fair to say in hot humid climates that the biometeorological success of any building design depends primarily on correct window design.

Ventilation rates will of course be greatest on the side of the building facing the direction of the wind. Where good natural ventilation is important, windows should face the prevailing breeze, account being taken of deflections of the prevailing air stream by topographical features, and by nearby buildings (see Fig. 98).

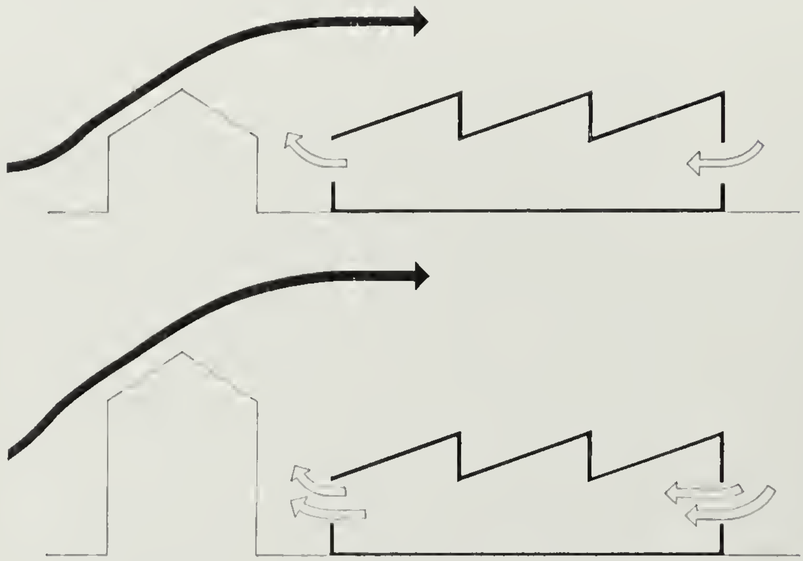

Fig. 98.
The pattern of air flow through buildings must be determined by observation and not by speculation. Obstructing buildings may make the air move in the opposite direction to the free wind. Better ventilation may result from obstruction by a high building (below), because of the more intense zone of low pressure in its lee, than by a low building (above). Based on studies by L. T. Weston.

Sunshine and radiation in buildings

The discovery of the connection between sunshine and rickets and the claims made for ultraviolet therapy for tuberculosis etc. have so coloured the general medical and popular attitude towards sunlight, that it is difficult to get a balanced scientific assessment of the role of sunshine in building hygiene today: It is probably fair to say that sunlight is desirable in winter when the weather is cold, and undesirable in summer when the weather is hot. This would seem to indicate that sunlight is valued primarily as a radiant heat source. As virtually no ultraviolet light penetrates normal glazing, the physiological effects would seem to be mainly restricted to the "euphoria" which results from sitting in a pleasant radiant environment.

Direct sunshine becomes unpleasant enough, once the air temperature begins to rise in summer.

The problem of sunshine in buildings would therefore seem to fall into three parts: (*i*) The provision of adequate sunlight in winter. (*ii*) The control of excessive radiant heat gains in summer. (*iii*) The regulation of the brightness patterns which occur which tend to interfere with good seeing conditions in the interior.

Favourable orientation[1097] can do much to solve the first two problems. Facades facing the equator show three great advantages (except at very high latitudes). Firstly the radiant gains are considerable in midwinter. Secondly the radiant heat gains at midsummer tend to be appreciably less than at the equinoxes, the high summer sun falling very obliquely on the glass surface making the heat gains small. Thirdly protection by suitable shading devices is much simpler than on other facades. Heat gains on the west facade in summer are particularly difficult to control satisfactorily.

The illumination problem is best handled by the use of suitable diffusing blinds to reduce interior brightness contrasts.

The daylighting of buildings

The daylight available in a building depends on the local outside illumination climate, and on the practical use made of it. At the back of rooms illumination intensities of the order of 0.5–2% of those found in the open are typical. There are two basic problems in daylighting design, firstly to provide sufficient illumination for the type of task to be carried out and secondly to try to reduce any excessive contrasts of brightness which will give rise to glare[4079, 4080]. Any practical solution has also to take account of the thermal balance of the building. Excessive glazing tends to make buildings cold in winter and hot in summer. The basic problems to be faced in design vary from climate to climate. In high latitudes little daylight is available on overcast days in winter. Such winter days represent the typical design condition. In lower latitudes there may be plenty of light, and the problem becomes much more one of control of glare, and prevention of excessive heat gains. In desert climates the main sources of glare are the bright sunlit ground, and facades of other buildings. The blue sky in such regions is usually of very low luminance. In hot humid climates the sky itself usually is very bright (due to interreflection of sunlight from clouds) and special precautions must be taken against sky glare either by using specially designed overhangs, or by using tinted glasses to reduce the brightness of the sky. Poor daylighting leads to eyestrain, loss of working efficiency, headaches and often general malaise. Daylighting design has therefore considerable medical significance.

Dampness in buildings

Dampness in buildings is supposed to contribute to all sorts of medical ailments, but it is often difficult to find concrete evidence of the precise medical significance of dampness in buildings (see pp. 35, 216 and 223). Dampness in buildings is usually a sign of neglect. It often provides an indication of a general decline of environment that is likely to be reflected in all aspects of living, including sanitary habits and diet. Excessive dampness is often associated with lack of heating and the traditional link between words cold and damp may be significant. This may be one of the reasons why hygienists consider damp as such a bad portent.

Section 5. Biometeorological Principles to be considered in the Location, Design and Construction of Hospitals and Sanatoria

(see pp. 505, 616, 642–647, 679)

1. General Hospitals

General hospitals are called upon to treat a multitude of conditions most of the patients tending to stay a comparatively short time. Considerations of ease of accessibility, ease of visiting, staff recruitment etc. usually lead to an urban location. If peripheral sites are selected, transport may become an acute problem, and the majority of large hospitals tend to be in the centres of large towns on grounds of convenience rather than health. The investment per bed is usually high, and it is often possible to equip whole wards with special airconditioning equipment for various purposes to transform the climate. For example, wards exist in London for the treatment of patients affected by severe smog; the air is filtered and chemically treated. In Liverpool a special ward for the treatment of childrens' burns has been erected. It is conditioned to give a hot dry, desert-like atmosphere, in which it is claimed burns heal more quickly.

Good site selection will offset some of the meteorological shortcomings of central urban areas. The obvious sites to avoid are the highly polluted ones. Sunshine is much appreciated by patients in high latitudes and orientation to the equator side in such regions is often an advantage. Where there are cool or cold winters, slopes facing towards the equator are to be preferred, to slopes facing polewards. The greater insolation makes the environment warmer, and there is less risk of overshadowing. Damp, low lying ground should be avoided on account of fog and mist and also very exposed sites on hill tops. The space about the buildings is valuable for convalescence and with careful thought, it is possible to plan outdoor spaces protected from wind, where patients can sit during the later stages of their recovery, enjoying sun or shade according to season. The proximity of nearby parks may improve general amenity and reduce pollution.

In the tropics there are considerable advantages in choosing sites that enable the long axis of the building to be run east-west, so the main facades face north and south. These north-south facades are easy to protect from sun. The west orientation in particular is unsuitable for hospitals in warm climates. Protection from the sun is difficult on this orientation, and the risk of overheating is considerable.

The significance of sunshine in modern hospital building is not exactly clear. Undoubtedly, in cooler climates, it is appreciated psychologically by the patients. Its bactericidal value is open to some doubt, if ordinary glass windows are used, for these absorb practically all the ultraviolet light. The same comments apply to its value for ultraviolet therapy, unless outdoor spaces for patients beds are provided. The high levels of illumination from sunshine undoubtedly show up dirt and dust, and it may be one of the contributions of sunshine to help encourage a cleaner environment.

When it is decided to modify the environment internally for the benefit of patients, it is necessary to form a clear idea of the shortcomings of the existing environment, and to decide on some order of priority, as it is difficult to suit the needs of all the patients in a general hospital. It is not necessary however to have the same environment throughout the hospital, for some patients air filtration and chemical treatment of the air supply may be desirable, for others a cool environment in hot weather and so on.

2. *Special Hospitals and Sanatoria*

Special hospitals and sanatoria tend to deal more with chronically sick patients than acutely sick, and hence the need for central location is less important. Accessibility however should not be overlooked in site selection. Rural sites which appear attractive in summer, may be depressing in winter. The isolation may make it difficult to get and keep staff, and the patients may feel the lack of contact with their friends and relatives. Clean small country towns with relatively unpolluted air can often offer a combination of a healthy site and urban facilities which makes them more suitable for practical purposes than very isolated rural areas. Good sites, favourably oriented with suitable grounds can often be found on the outskirts of such towns, and the construction of special hospitals can often be carried out in single storied construction which makes it easy to move the patient from his indoor environment to the outdoor air. It is important that a proper biometeorological assessment should be made of the climate, for a few fleeting visits can be very misleading. A study of local climatological data should reveal the times of special stress, and, if they are not so severe as to make the site inacceptable, what precautions to take to alleviate them by proper building design and construction. The chronically sick often favour a mild external environment, and it is often possible to engineer a favourable outdoor microclimate by use of walls to break the breeze, trees to provide shade in hot weather, and so on. Advantage can be taken of favourable orientation to provide sun traps where patients can sit in comfort in the early spring and late autumn.

Medical practice differs so much from one part of the world to another, so it is almost impossible to make general architectural recommendations to cover the treatment of specific diseases. For example, sun therapy is favoured in some countries for the treatment of tuberculosis. In other countries, excessive sunshine is considered detrimental to recovery. In summarising biometeorological aspects of allergic diseases, Dr. Alemany-Vall showed the evidence was very conflicting, and that it is difficult on existing knowledge to choose locations favourable to asthmatic patients as a group[4078]. A climate which suits one patient may not suit another.

Fashion has always played an important part in the location of hospital facilities for the chronically sick, especially for the rich. Physicians, however, should be careful to distinguish between scientific evidence, and fashionable opinion in considering the climatological advantages of particular sites. Bad building design can probably do more to create an unfavourable environment than anything else, and adequate treatment can often be secured without the need to remove the patient from his home town, provided buildings are properly designed, and are suitable for the climate.

CHAPTER 4

Social Biometeorology

A definition of Social Biometeorology and of the three principal subdivisions was given on p. 10, *viz.*, General Social Biometeorology, Psychological Biometeorology and Archeological Biometeorology. Only the first two will be discussed in greater detail. The third, the study of the possible influence of weather and climate on the origin, distribution and disappearance of past civilisations, is a fascinating subject but so far little accurate information is available.

Section 1. General Social Biometeorology

General Social Biometeorology, in France better known as *Climatisme Social*, comprises the study of the influence of weather and climate on the community and its application, both in a preventive and curative sense. Considering the influence of weather and climate on diseases such as rheumatism and bronchial asthma, and the social implications of these diseases (see pp. 466 and 545), the study of various measures taken in the field of climatotherapy for reducing or curing serious "social diseases" has been included in General Social Biometeorology.

Problems related to the best location and construction of recreation camps, revalidation centres, sanatoria and clinics required for these "social diseases" belong to this field. This aspect has just been discussed by Page in the previous section. Despite its significance, very little scientific work has been carried out in the field of General Social Biometeorology. A large number of practical empirical rules has been found but the scientific basis for many of the conclusions is mostly lacking. However, for future work use should be made of the various meteorotropic observations described in the previous pages for the different diseases to enable us to establish biometeorological rules governing the location and construction of sanatoria or clinics for certain diseases.

Section 2. Psychological Biometeorology

Psychological Biometeorology comprises the study of the influence of weather and climate on the mental processes of healthy man. The study of the influence on mental diseases (described on pp. 534–545) belongs to Pathological Biometeorology. A special branch of Psychological Biometeorology, known as *Aestheto-Biometeorology,* studies the influence of climate and weather on the aesthetic expression of man. The latter aspect will not be discussed in this section.

Only a brief review will be given of the following interesting meteorotropic psychological studies which may have some practical social and clinical implications: Biometeorological Typology (*i.e.* the possible influence of the psychological pattern of man on kind and degree of meteorotropism); Reaction speed, working efficiency and accuracy of work; intelligence and restlessness of schoolchildren; traffic and industrial accidents.

1. *Biometeorological Typology*[4102–4108]

Many biometeorologists are inclined to believe that the type of meteorotropism observed in man is closely related to his body build and psychological pattern. This concept, known as biometeorological typology, was introduced and defended by Curry[4102, 4103] more especially. Although undoubtedly a number of physiological observations seem to support the general concept, a simple typological classification as suggested by Curry cannot be accepted.

Curry classified people into two groups, the *K (cold front)-type* and the *W (warm front)-type.* The typical K-type represents the pale, introvert personality, often with thin long limbs and narrow face. These people, he maintains, are very sensitive to the influx of cold air and cold fronts. They are inclined to have an overstimulated parasympathetic nervous system. The typical W-type is characterized, according to Curry, by an extrovert personality, shorter and fatter limbs and a round face. They are particularly sensitive to warm weather conditions, warm fronts, and the influx of warm tropical air. They are inclined to have an overstimulated orthosympathetic nervous system. The typology described corresponds more or less to Kretschmer's classification and the extended classification by Sheldon[4107, 4108] used in anthropobiology. The typcal K-type seems to correspond to Sheldon's *ectomorph type*; the W-type is similar to his *endomorph type.*

The assumption that the same weather conditions could have different meteorotropic effects is supported by the following observations:

(1) *Data collected by constitutional psychology.* Sheldon defined constitutional psychology as the study of the psychological aspects of human behaviour as they are related to the morphology and physiology of the body. Not only the psychological pattern of, but also the natural resistance to, particular diseases appears to be related to Sheldon's somatotypes. This

assumption was expressed first by Draper[4103a] and is known as the *immunity panel of personality*. According to Draper, gall bladder patients tend to be of thick and stocky build, whereas gastric ulcer patients tend towards linear development. His observations (mainly at the N.Y. Presbyterian Hospital) were supported by Sheldon. On a statistical basis peptic ulcer seems to be most frequent in Sheldon's somatic type 244, whereas gall bladder patients are most frequent among the mesomorphic endomorphs (a true mesomorph is the muscular athletic type). It appears that relatively few cases of cancer occur among mesomorphic ectomorphs. Although Sheldon's conclusions are based on very extensive clinical material, considerably more evidence is required before a specific somatic type can be definitely correlated with a high incidence of a specfic disease. Nevertheless, it does look from the available evidence as though weather stress affects different somatic types in different ways.

(2) *Influence of personality pattern on thermoregulation processes.* A number of accurate scientific studies were described on p. 229, indicating that, depending on personality pattern and body build, different results are obtained from thermoregulation tests. This variation tallies with the fact that basal metabolism is related to surface area of the body and sex (see p. 212) and with the biometeorological rules described on p. 445. The studies of Petersen and Sargent (see p. 526) suggest a relationship between common cold, weather and body habitus.

(3) *Influence of body morphology on pulmonary ventilation.* As noted on p. 300 Seltzer described a difference in oxygen consumption and pulmonary ventilation in healthy persons, depending on their body morphology.

(4) On p. 201 the *influence of individual differences in physiological pattern* on acidity of the blood, potassium-calcium ratio, etc., as observed by Hoff[500-503] were described.

In view of these various observations suggesting a close relationship between certain physiological processes, predisposition to certain diseases, body build and psychological pattern, it is logical to assume that different human types will react differently to the same weather stress. The observations described on pp. 207–255, in particular, concerning the thermoregulation processes and the great significance of these processes in many meteorotropic phenomena support the view that future detailed work could probably build up a biometeorological typology which would be of great clinical value.

2. *Speed of Reaction, Working Efficiency and Accuracy of Work*[4109-4123]

Several reports have been published on the possible influence of weather and climate on the speed of reaction and working efficiency, but only very few of these studies can survive critical statistical analysis.

On p. 244 it was stated that, under extreme heat stress, working efficiency in the Navy decreases. Bedford[4109], Moss[4115], Vernon[4118-4121], Weston[4122] and others described similar observations in coal mines, heavy industries and weaving mills. Mackworth[4114] studied the performance of 11 experienced wireless telegraphy operators at temperatures ranging from 87 to 97° F. Hot and moist air seriously impaired accuracy. However, some authors believe that a change in reaction speed and labour efficiency may also occur under non-extreme conditions, due to over- or under-stimulation of the autonomic nervous system as a result of weather stress.

The first accurate study was carried out by the German physicist Reiter[4117] in 1953 during the Traffic Exhibition in Munich. On 71 days, 53,000 visitors were tested for their speed of reaction. A total of 210,645 observations were made with a daily average of 1700–4500 recordings. The test was very simple and reproducible. It was found that on days of strong disturbances of electromagnetic long waves (see p. 80) a statistically significant decrease in speed of reaction was observed. No correlation was found between the passage of fronts and foehn weather.

Similar correlations were found by Düll[4111] in 1941, and in recent years by Brezowsky and Ungeheuer in Bavaria, using the weather phase method (see p. 24).

In 1953 Vermeulen tested for one year the accuracy of a group of experienced female chemical analysts working in the same laboratory near Oosterbeek (the Netherlands). A statistically significant decline in accuracy was observed in April, lasting through the early spring.

3. Intelligence and Restlessness of Schoolchildren

Studies by Ungeheuer[4124] and others suggest that fluctuations in restlessness and comprehension can be observed in schoolchildren on certain days, or during certain periods, which cannot be explained by ordinary psychological factors. A comparison with weather phases (p. 24) gave a statistically significant correlation between days or periods of restlessness of children and drastic changes in weather conditions. The sudden increase in their restlessness shortly before thunderstorms, which are usually preceded by high temperatures and humidities affecting the thermal comfort of children, is easier to understand than a general weather relationship. More studies are required to confirm the observations of Ungeheuer and others. The possible influence of season and the month of birth on the I.Q. of children was already briefly mentioned on p. 535.

The influence of *sea climate* has been reported by a number of research workers. Berliner[3713] observed in children at Norderney (Germany) a greater speed of calculating arithmetical problems and a higher accuracy after a few weeks of thalassotherapy. On the other hand the degree of attentiveness was reduced. In other children colonies more landinwards this psychological change was not observed. Muchow[3981] could confirm the observations of Berliner at Wijk/Föhr (Germany). Shortly after sea and heliotherapy calculating speed and accuracy increased, attentiveness decreased; after heliotherapy only all three increased; after walking in strong wind all three factors decreased. Similar observatons were made by Petrasch[3996] and Langelüddeke[3958].

4. Traffic and Industrial Accidents[4125–4136]

Most authors who have studied the possible influence of weather on accidents are inclined to believe that, if such a relationship exists, the relationship is an indirect one due to the influence of weather on the driver's or operative's speed of reaction. Reiter[4129, 4130] studied 362,000 industrial accidents in Bavaria, Württemberg and Hessen (Germany) in the period of 1950 to 1952. A statistical analysis demonstrated a mathematically significant relationship between weather and industrial accidents. On days of considerable disturbance of the electromagnetic long waves the number of accidents increased by 20–25%.

A similar analysis was carried out by Reiter[4137, 4138] between July 1949 and June 1950 of 21,000 traffic accidents in Bavaria (Germany) and it was found that a statistically significant increase in the number of traffic accidents occurred during days or periods of electromagnetic disturbances. As indicated on p. 674, according to Reiter such periods are also characterized by a decrease in the population's average speed of reaction.

The influence of thermal stress on industrial accidents was described by Bedford[577], Vernon[4120] and others. Vernon studied the daily number of accidents in a large munitions factory during the 1914–1918 war. It appeared that accidents were least frequent in periods of environmental temperatures of 65–69° F. Below 65° or above 69° F accidents increased in frequency. Compared with the rates of the 65–69° interval, above 75° F the mean accident frequency was 23% greater, below 55° F even 32–35%. Studies in coal mines showed a similar temperature relationship. Work done for two years by Vernon, Bedford and Warner in 1927[4132], during which they analysed the accidents (causing over 3 days' absenteeism) incurred by 18,000 underground miners in England revealed that most accidents occurred at the warmest places in the mine, *e.g.* at the coal face. The number of accidents among coalface miners working at 80° F was 30–77% higher than those working at temperatures below 70° F. For other underground workers the temperature effect was even more pronounced. The accident rates above 70–74° F (as compared with those below 70° F) were 42–50% higher, above 75° F the excess was 61–72%. Not only the number of accidents increased but also the severity in terms of the number of days lost on account of accidents per one thousand working hours. Age group studies revealed that with increasing temperatures a more rapid increase occurs among the older age groups.

This brief summary of a number of important problems in the field of Social Biometeorology warrants a further extensive study of this rather neglected field. Despite the fact that the various observed statistical relationships do not have to be causal, the high degree of statistical significance observed in several of the studies described suggests that at least some of the correlations may be true relationships. Also, the problems related to month of birth and mental deficiency (see p. 535), sexual ratio (see p. 570), mortality (see p. 571), birth frequency (see p. 569), etc., have considerable social implications and should be included in a future scientific study of Social Biometeorology.

PART V

Effect of Weather, Climate and Season on the Living World Surrounding Man

CHAPTER 1

Effect on Plants (Phytological Biometeorology)

A vast amount of literature has been published on the influence of weather and climate on plants, particularly in the field of *agro-meteorology* (*i.e.* the study of the influence of meteorological factors on agricultural plants). It would be outside the scope of the present book to try to review some of the most important discoveries made in this field. Only a few observations will be mentioned which are of direct significance for man and animals.

(1) It is known that, owing to the photochemical action of sunlight on the chlorophyll bodies in cytoplasm (particularly wavelengths between 490 and 760 m μ, *i.e.* green to red), carbon dioxide in the air, together with water, is converted into carbohydrates and oxygen, a process known as the *assimilation* or *photosynthesis* of plants. As a result, during the day the atmosphere in the immediate surroundings of plants or trees may become poorer in CO_2 and richer in oxygen. This process of assimilation depends on the structure, shape and number of chlorophyll bodies in the plants, the temperature and humidity of the air and the intensity and prevailing spectrum of sunlight and air movements.

A plant must also be able to *breathe*, apart from assimilating CO_2. It absorbs oxygen from the air and breaks down the carbohydrates formed during photosynthesis into CO_2 and water. Owing to this breathing process, most plants are able to produce 5–10 times their volume in CO_2 in 24 hours. A rise in temperature of 10° C doubles or triples the CO_2 production. Therefore, a rich vegetation surrounding the living quarters of man will affect the oxygen-carbon dioxide ratio of the air, which is influenced by the temperature, hours of sunshine and wind speed of the environment.

(2) Forest vegetation in general has a number of important biometeorological effects upon the local micro-climate: (*i*) It increases the moisture of the air, which in turn reduces the number of small ions (see p. 71), increases the number of large ions and reduces the electric conductivity of the air (see p. 72). (*ii*) It reduces air movement and general air turbulence. (*iii*) It reduces the amount of direct or reflected solar radiation reaching the air near the soil. (*iv*) It reduces the degree of air pollution by chemical compounds and inorganic particles. (*v*) The air above the soil usually does not

cool off as rapidly during clear nights as in open fields and this may prevent the formation of ground mist. (*vi*) The electric potential gradient (and the daily fluctuations) in a forest is very small (see p. 76).

In a word, forest vegetation tends to temper various meteorological factors and therefore reduces some forms of weather stress. Whereas in many instances this may have a favourable effect on diseases, a forest climate may be detrimental to certain forms of psychiatric diseases which require stimulation of the autonomic nervous system.

(3) The indirect influence of weather on plants and man, through changes in the *vitamin* and *trace element* contents of food, was reviewed on pp. 581–584.

CHAPTER 2

Effect on Animals (Zoological Biometeorology)

On p. 455 the experiments of Schua and Reiter were described suggesting the possible influence of fluctuations in the electric field of the atmosphere on golden hamsters and guinea-pigs. Considerably more biometeorological work has been carried out, pertaining to temperature and cooling, on other groups of animals, of great economic or medical importance to man. Biometeorological work has also been done in relation to animal hibernation and reproduction, throwing further light on similar physiological processes in man.

It is beyond the scope of this book to review all these studies, but a few important observations will be briefly mentioned. This chapter is divided into four sections: (*i*) Domestic and farm animals; (*ii*) Birds; (*iii*) Insects as vectors of disease (by Dr. Haufe, of Canada); (*iv*) Hibernation and reproduction of animals (by Prof. Folk, of U.S.A.).

Section 1. Domestic and Farm Animals

Various aspects of zoological biometeorology have been studied.

Subsect. A. THE THERMOREGULATION SYSTEM OF ANIMALS

An excellent summary of this problem was given by Christophersen, Precht and Hensel[672].

A domesticated *swine* seems to be more affected by summer temperatures than other farm animals, because it is a non-sweating animal and, in addition, with increasing weight the fatty covering acts as a barrier to the loss of body heat. With rising environmental temperature the respiration rate in swine rises rapidly (for further details see T. L. Noffsinger and F. N. Andrews, *Intern. J. Bioclimatol. Biometeorol.*, *3*, 3C, 1959 and J. D. Findlay, *Bull. No. 9, Hannah Dairy Research Inst.*, Scotland, 1950).

A considerable amount of work has been carried out on the *heat balance of cows* by Findlay *et al.* in Scotland (*Environmental physiology of farm animals*, Progress in the physiology of farm animals, *1*, 252–298, 1954). They were able to show that cows are better adapted to low than to high temperatures, the comfort zone for cattle being between 0 and 15° C. The main reasons for ill-adaptation of cattle to hot environments are the following: (*i*) The *high level of heat production*: in a non-lactating, non-gestating cow it amounts to 10,000 kcal/day; in a cow yielding 20 kg of milk per day it amounts to 20,000 kcal/day. (*ii*) *Poor sweating facilities of cows*: the skin moisture evaporation reaches a maximum at only 17° C ambient temperature (according to Kibler and Brody).

Cattle of northern latitudes feel uncomfortable when exposed to sun without wind. The grazing time of temperate breeds of cattle is very much less than of tropical breeds. When temperate breeds of cattle rest, they never do so in the sun, whereas tropical breeds never lie down in the shade. The effect of solar radiation in the tropics is greatly affected by the coat covering. A white, yellow or red coat with a smooth and glossy texture considerably minimizes the effects of solar radiation (according to Findlay).

The difference in heat regulation between tropical and temperate cattle shows up particularly in the *respiratory frequency* which increases steeply in temperate cattle with rising environmental temperature (especially above 15° C), whereas the increase is more gradual in tropical cattle. This is partly due to the fact that the surface area to body weight ratio of tropical cattle is about 12% greater than of temperate cattle. The *heart rate* usually increases steeply above 25° C (in temperate cattle); the *rectal temperature* above 30° C. This holds only under conditions of low humidity. With great humidity the rise starts erlier and is more precipitous. Thermal stress also affects the *blood composition* of cattle. At air temperatures of 18–40° C there is a large increase in the creatinine content of the blood; the carbon dioxide combining capacity, the ascorbic acid and cholesterol levels in the blood are reduced to less than half the levels at 10° C. Unlike man, there are no disturbances in the water, electrolyte balance or colloid concentration. This is probably due to the fact that in man, above 27° C, the evaporation loss rises exponentially with increasing temperature, whereas there is no increase in cattle.

Heat stress also affects the *reproduction rate* of animals. In sheep it decreases under great heat stress. Warming of the scrotum of a ram causes panting and stress on the thermoregulation system. In this connection it is interesting to note that in the general population, man's reproductivity is also reduced in very hot regions or after very hot summers.

Studies by Harrison *et al.* (*Phil. Trans. Roy. Soc. (London), B*, *242* 479–516, 1959) confirmed observations of other workers that mice reared at high temperature have longer tails than those reared at cold temperature. Mice reared in the heat also survived longer in a hot, humid environment.

According to Hutchinson, the higher the mean temperature the more "leggy" are the breeds of cattle.

Subsect. B. INFLUENCE OF WEATHER AND CLIMATE ON MILK YIELD

1. *Direct Influence*

When cattle are exposed to great thermal stress, milk production may decrease by 50–75%. Also, food consumption decreases (Findlay). Oosterlee observed in the Netherlands that the milk yield of cows with a normal milk production (20 kg milk/day), housed in open sheds, was unaffected during periods of very low temperatures, provided their food be not frozen. However, in closed barns the milk yield of cows with a low level of production decreases during frost. The greater solar irradiation in the open sheds may be one of the reasons for this difference.

2. *Indirect Influence (depending on Construction of Cow Stalls)*

Experiments by Oosterlee in the Netherlands indicate that non-evaporative cooling of cattle is higher when an animal is lying than when standing, provided the floor of the stall be well-insulated. Therefore, in cold climates such insulation is highly to be recommended. A small layer of straw on the floor of a stall reduces the flow of heat to the ground beneath from 150 kcal/m^2/h to 40 kcal. In warm climates the floor insulation should be poor to increase the animal's comfort and milk yield. Oosterlee pointed out that, especially in spring, temperature and humidity conditions may prevail in cattle stalls resembling tropical conditions, which may cause a considerable drop in the milk production.

Subsect. C. INFLUENCE OF WEATHER AND CLIMATE ON THE ANIMAL'S COAT

J. C. Bonsma (*J. African Sci., 39*, 204–221, 1949), J. C. D. Hutchinson *(Congress Proceedings of the 2nd Intern. Bioclimatol. Congr.,* London, Sept. 1960, Pergamon Press, Oxford, 1962) and others found a close correlation between the coat character of beef cattle and their heat tolerance. This in contrast to sheep, in which such a correlation does not seem to exist. As a result the woolly Australian Merino is found well into the tropical regions of Queensland.

The following observations were made in beef cattle in Australia:

In semi-arid tropical regions well-adapted animals have a smooth sleek coat.

Yeates (*Australian J. Agricult. Research, 6,* 891–902, 1955 and *8,* 733–739, 1957) showed that coat shedding in spring is controlled by day-length. Poor nutritional conditions delay the spring shedding.

In January and February (warm period) the mean coat score in Australia is low for various cattle breeds (*i.e.* the coat resembles a coarse sleek Zebu type of coat). From May till September the coat score is high (*i.e.* a woolly coat).

The coat score and skin temperature, measured in hot weather in shaded positions on the trunk, indicate an increasing coat score with rising skin temperatures.

The coat score of calves, during 10 months after weaning, seems to increase with decreasing gain in weight.

According to Turner and Schleger, the calving rate and birth weight of calves are related to the coat score at the time of mating of the cows. With very high coat scores the cows failed to calve.

It was found that clipped animals would grow much faster (about 14%). This is probably partly due to the insulating properties of the coat against temperature and radiation.

The long fleece of sheep acts as a protection against solar radiation and increases the heat tolerance of the animals. Macfarlane recorded in the sun temperatures at the wool tips of 87° C against 47° C on the skin. Shorn sheep also pant twice as fast as animals with 5 cm fleece. In other words, a high coat score increases the heat tolerance of sheep, whereas it decreases the heat tolerance of cattle. This seems to be due to the higher rate of sweating of cattle as compared with sheep. In sheep, panting is more important for their heat regulation.

Subsect. D. INFLUENCE OF WEATHER, CLIMATE AND SEASON ON ANIMAL DISEASES (PATHOLOGICAL ZOO-BIOMETEOROLOGY)

Both direct and indirect influences are known, the latter being more generally recognized.

1. *Indirect Influences*

Weather, climate, season and soil determine the type of plants growing in a particular area and their chemical composition (particularly trace element and vitamin contents). As animals, more than man, live largely on the food grown in the immediate surroundings of their living quarters, local changes in weather and climate may affect the nutrition of animals and are therefore responsible for various metabolic disorders and deficiency diseases observed in farm animals.

Poisonous plants and toxic fungi in meadows may also cause animal diseases. The abundance or scarcity of such plants and the severity of the poison often depend on specific weather conditions. An example of such a meteorotropic disease is that known as *facial eczema* in New Zealand, a liver disease common among sheep, but also liable to attack cattle and horses. The liver damage is caused by a photodynamic substance (see p. 350), phylloerythrin, a product of the digestion of chlorophyll in ruminants, which normally is eliminated in the bile. However, when it damages the liver, it reaches the peripheral arteries and, upon exposure to sunlight, severe skin lesions occur. Recently it was found that the liver injury is due to a toxic fungus in certain rye grass pastures in New Zeland. The development of the fungus (and of the disease) is clearly seasonal. Outbreaks occur in autumns which follow a hot dry summer. It seldom occurs after a cool wet summer or during a late cold autumn. Outbreaks occurred particularly after rain (only $^1/_2$ inch is required) which stimulates the new growth of dried-up pasture. Supported by present knowledge, Filmer, Mitchell, Walshe and Robertson were able to develop a system of meteoropathological forecasting for this particular disease.

2. *Direct Influences*

An excellent summary was published by M. Crawford in the *Congress Proceedings of the 2nd Intern. Bioclimatol. Congr. London,* Sept. 1960, (Pergamon Press, Oxford, 1962). Although some of the diseases mentioned below are, strictly speaking, not "directly" due to weather, the meteorotropic influences are of a more direct nature than those mentioned above.

(1) *Grass tetany* is a disease characterized by tetanic convulsions frequently causing death. It is due to hypomagnesaemia (see p. 276). It is common in grazing cattle and sheep if the magnesium content of grass falls below a certain level. The disease is being extensively studied in England by Allcroft *et al.*[458, 1261–1269] and in the Netherlands by 't Hart and Kemp. The specific meteorological conditions which seem to activate the magnesium deficiency have already been discussed on p. 276.

(2) *Anhidrosis of horses* occurs particularly in racehorses imported from temperate zones into tropical areas of high humidity. The animals lose the ability to sweat when exercised, even in very hot weather. They finish a

race with a dry skin, with a serious disturbance of the thermoregulation mechanism as the result. The body temperature may rise to 110° F and the horse may die.

(3) *Tick-borne diseases* constitute many of the diseases attacking livestock. The ticks increase in number and size under specific meteorological conditions of temperature, humidity and solar radiation. Their survival depends on compensation at night for their loss of water during the day and this, again, depends on the humidity of the air and the availability of dew.

(4) *Bacterial diseases. Braxy* is a very acute fatal disease in sheep caused by infection of the stomach and intestinal wall by a sporulating organism *Clostridium septicum,* which is common in soil. Although regularly contracted by grazing sheep from the soil, usually sudden deaths only occur with the onset of the first severe frosts in late autumn and early winter. Apparently, a chilled stomach resulting from the ingestion of very cold grass facilitates the invasion of the bacteria. *Haemorrhagic septicaemia of cattle,* caused by *Pasteurella septica,* occurs in India and other parts of Asia soon after the onset of monsoon rains. It has been assumed that the sudden flush of young grass after the shortage of food in the long dry summer upsets the digestive system of cattle.

(5) *Virus diseases.* Some of the animal virus diseases are transmitted by insects and therefore depend on the weather-insect relationship (see p. 689). A good example is *Rift valley fever,* affecting sheep in particular, but also goats, cattle and man. It is widely distributed in Africa and is transmitted by a mosquito. It develops in summer and autumn in the wet seasons in valleys and other low-lying areas. Another example is *Foot and mouth disease,* one of the most highly infectious animal diseases, which seems to affect cattle in good condition with the greatest severity (Crawford). In cattle in poor condition the disease is generally mild and the lesions are small and inconspicuous. Crawford and others observed that in tropical countries it is much easier to prevent the spread of this disease from an infected herd. It seems that the virus does not easily survive excessive sunlight and high temperatures, whereas the damp cold weather of W. Europe favours its survival and the spread of the disease. Experiments conducted by W. Kötsche (*Arch. Exptl. Vet. Med., 13,* 141–156, 1959) on mice infected with foot and mouth disease indicated that the morbidity decreased when high atmospheric pressure, low humidity and low temperature prevailed. Experiments by L. D. Marshall (*J. Hyg., 57,* 484–497, 1959) demonstrated the importance of the general resistance of the animal (see p. 513) also in the case of foot and mouth disease. Seventy percent of rabbits

infected with a strain of virus causing myxomatosis recovered at summer temperatures, whereas only 8% did so at winter temperatures.

(6) *Liver fluke disease or fascioliasis*, is a dangerous disease in sheep resulting from damage done to the liver by the trematode (a kind of worm) parasite *Fasciola hepatica*. The parasites have a very complicated life cycle in which the snail *Lymnaea truncatula* plays an important part. In 1959, after ten years of field work, Ollerenshaw and Rowlands were able to show that specific humidity and temperature conditions are required to make this cycle a success and to cause bad "fluke years".

The observed weather relationships are not merely a matter of theoretical interest. Further study of the phenomena described may enable the veterinarian and meteorologist to predict the outbreaks of these diseases. Needless to say, if such accurate meteoropathological forecasting could be developed, it would be an immense economic asset to countries with a high percentage of domestic and farm animals.

Section 2. Birds

Weather and climate influence birds indirectly through food and directly to the extent that certain meteorological factors (particularly temperature and solar radiation) affect the production of sexual hormones (see pp. 261 and 570), the sexual ratio (see p. 265), the laying rhythm of fowls, etc. According to some authors, weather and climate affect the colour and appearance of the feathers. Also, the direction-finding capacity of migrating birds has been ascribed by several research workers (*e.g.* Kramer in Germany) to the capacity of various animals to locate themselves by means of the rays of the sun, their direction, intensity and degree of polarization (see p. 349).

From a practical point of view the most important studies have been carried out in relation to season and the laying rhythm of hens. An interesting summary was published by M. V. Albada (Seasonal and lighting influences on the laying rhythm of the fowl, *Intern. J. Bioclimatol. Biometeorol., 2,* 3A, 1958). He pointed out that, whereas in wild birds the laying of eggs is limited to a few months in spring time, prolonged domestication and selection have extended the period of egg production in the domestic fowl to the entire year. For all that, many domestic fowls are sensitive to seasonal influences. Thus the laying results in temperate zones of the northern and southern hemispheres indicate a *maximum production in spring*, whereas in the tropics the production is equal throughout the year. However it should be borne in mind that part of the spring peak is due to the limitation of the hatching season to the months of spring.

Investigations have shown that the change of hours of daylight is a dominating factor in the seasonal effect on laying rhythm. Light stimulates the pituitary. It secretes follicle stimulating hormone (see p. 257). Hens' ovaries are stimulated to activity and the egg follicles develop and mature. The almost mature follicle sends a, probably hormonal, stimulus to the hypophysis, under the influence of which the latter causes the follicle to complete maturity and ovulation. Between the secretion of the ovulation-inducing hormone and ovulation itself a fairly constant period of about 8 hours elapses. For further details concerning the effect of the length of day and the intensity and composition of light on egg cycles and egg production the reader is referred to Albada's article.

It is not only the egg production which is affected by season, but the age at which *sexual maturity* is reached as well. In the northern latitudes it is well known that "early" pullets, hatched between January and March, will reach sexual maturity earlier than "late" pullets, hatched between March and May.

Section 3. Insects as Vectors of Disease

by

W. O. HAUFE

The main objective of entomologists in agricultural and medical research is to predict and to prevent outbreaks of insects that directly or indirectly compete with man in his environment. Epidemiology is the central problem in dealing with insect pests and consequently studies must ultimately be based on an ecological point of view. The ecological concept of entomology, in medical, agricultural and economic fields alike, consists in recognizing the injurious insect as an intregal part and as a product of its environment. These considerations lead to the conclusion that living insects must be studied in relation to physical factors in climate and weather. This view is not original and, although adequate analyses of environment present problems of formidable complexity, an enormous literature already exists, especially for insects in the field of agriculture. The early literature has been informatively summarized by Uvarov[1273]. Specific assessments of the importance of various factors and more critical appraisals of approaches in future studies are to be found in three recent reviews by Graham[1189], Wellington[1284], and Messenger[1241]. Students in insect bioclimatics are directed to these reviews for comprehensive discussions of the effect of the physical environment on insects.

The following account does not pretend to be complete for the role of biometeorological studies in the epidemiology of insect-borne diseases. An earlier survey of this problem has been reported by Martini[1235]. For extensive treatment of the relation of insects and their environment to the epidemiology of certain thoroughly studied diseases, the reader is advised to consult Buxton's detailed account[4161] of the natural history of tsetse flies and epidemiology of trypanosomiasis, and Muirhead-Thomson's concise account[4248] of mosquito behaviour in relation to the transmission and control of malaria in the tropics. The intention in this brief account is to point out only the important major relations of insect vectors to man and to disease organisms with special reference to the common physical environment, and to focus attention on the central problem. Discussion is limited necessarily to a few selected examples relating to the influence of climate on epidemics. As far as possible, the examples are also confined to the more thoroughly studied and most widely distributed diseases such as yellow fever, malaria, trypanosomiasis, and filariasis.

Subsect. A. THE RELATION OF INSECT VECTORS TO THE PHYSICAL ENVIRONMENT IN EPIDEMIOLOGICAL PROBLEMS

Bioclimatics is generally defined as the science of life and its relation to climate[4213]. Biological aspects include first, the investigation of the effects of climatic factors on development, behaviour, survival and reproduction of the organism, and secondly, the prediction of distributions and abundance of species in nature. Climatological aspects involve the recording and measurement of climatic factors in areas where the species occur and the analysis and comparison of data in correlations. Much emphasis in earlier literature has been placed on the limitation of the range of a species by such broadly defined controls as geographic barriers and climatic restrictions. More recent studies on medically important species of insects indicate that with changes in human activities, especially in relation to travel, emigration and industrial and agricultural development, the importance of geography is being steadily reduced. Biological balances with the environment and distribution ranges have to be frequently redefined with time and with the gradual accumulation of the literature[4161]. This fact, more than any other, emphasizes an increase in the amount of attention to biometeorological aspects of insect distribution and abundance[4284, 4287].

Man, his pathogenic organisms, and insect vectors are members of a community of associated species in a common physical environment for at least a part, if not the whole, of their life cycles. Biological contact is complicated by daily, seasonal, or annual exchanges of individuals between populations in different ecologically defined communities, often, in the case of winged insect vectors, over distances of hundreds of miles[1180 1182, 4211]. Each species in a community is constantly adapting to physical changes in its climatic environment and to biological changes in other simultaneously adapting co-existing species. Natural selection is manifest as the result of long-term operation of these interrelationships and climate has an all-pervading influence[4236]. These considerations portend formidable complexity in systematically analysing, fully integrating, understanding, and ultimately predicting epidemics of insect-borne diseases. Nevertheless, the problems must be recognized and defined in perspective if the accumulation of basic knowledge is to be of practical value.

In recent years, methods in biometeorology, as well as those in pure climatology, have been strongly critized on their suitability for the description and measurement of phenomena in insect studies. For example, *static* measurements in methods and techniques applied to essentially *dynamic* systems have been reviewed unfavourably for climatological[4284] and for biological[4141] investigations. Too little attention has been given to the periodic variation that is characteristic of most thoroughly studied biological systems. Several reviews[4151, 4157, 4202, 4222, 4210, 4214], show that rhythmicity is a feature of biological activity throughout the animal and plant kingdoms (see pp. 369–371). This widely observed characteristic of biological response is immediately apparent from a biometeorological point of view because factors in the physical environment of terrestrial organisms also have obvious periodicities corresponding to days, seasons, years and longer spans of time[4154, 4163].

The importance of these considerations can be appreciated more easily by tracing the development of basic approaches in the epidemiology of malaria, one of the most widely studied insect-borne diseases of man. From the time of Hippocrates to the 19th century, the epidemiology of malaria was largely concerned with circumstances and surroundings such as marshes and comets that seemed to produce intermittent fevers[4262]. This approach might be termed *circumstantial* epidemiology[4231]. With the discovery of the malaria plasmodium in 1880 and of its mosquito vector in 1897, studies became strictly devoted to the bionomics of parasite, mosquito and man with the consequent development of a *biological* epidemiology[4231]. As MacDonald[4231] has pointed out, even thoroughly investigated and well known biological data on malaria were inadequate in explaining some striking differences in the behaviour of the disease. In Ceylon the disease was fickle and liable to explode into devastating epidemics; but in W. Africa it was remarkably stable and epidemics occurred only on the fringes of malaria zones. A *mathematical epidemiology*[4231] is now being developed to meet the inadequacy of epidemiological data and of vector bionomics in this long-studied problem. The mathematical model includes chief elements as follows: (*i*) Anopheline density in relation to man; (*ii*) Average number of persons bitten by one mosquito during one day; (*iii*) Proportion of anophelines with sporozoites in their salivary glands; (*iv*) Proportion of these which is actually infective; (*v*) Probability that the vector will survive one whole day; (*vi*) Days required for completing the extrinsic cycle under local conditions; (*vii*) Proportion of the human population bitten by mosquitoes during one day; (*viii*) Proportion showing parasitemia; (*ix*) Proportion of (*viii*) who have received a single infective inoculum and who revert to the uninfected state in one day; (*x*) The incubation interval which is the average time in days from the ingestion of gametocytes by an anopheline to the appearance of infective gametocytes in a second case infected by it; (*xi*) The reproduction rate or the number of secondary infections originating from a single primary case, and (*xii*) The infant-parasite rates, and rates and counts of gametocytes in older individuals classified into three-month age groups.

Russell[4262] has pointed out that unless the anopheline vector is almost totally refractory, the variations in susceptibility are relatively minor factors in contrast to the importance of man-biting habits, food preferences and average life expectancy of the insect vector. Mosquito activity and biting tends to be imperfectly periodic[4192-4194, 4198, 4205, 4230, 4248]. The variation in periodism depends primarily on differences in physiological response among individuals and in transient adaptation to changes in factors in the physical environment[4210]. A mathematical model for the epidemiology of an insect-borne disease such as malaria is theoretically incomplete if time and rate of response is not recognized in the host, vector and parasite. In other words, epidemics can occur when the phasing of cyclic or rhythmic activities, especially in the vector, is sufficiently close for a high degree of host-vector and reservoir-vector contact and consequent parasite transmission. The meteorological and climatological environment has an important role in mediating these systems [4187]. Unpublished correlations on biting flies in subarctic Canada have shown that daily peaks of various activities are influenced and in many cases limited by factors in the physical environment. Obviously, bioclimatics pervade the chief factors in MacDonald's mathematical epidemiology, and all but (*xii*) among the factors listed are related at least partially to variations in vector activity. The striking differences in the incidence of malaria may depend largely on failure to recognize the dynamic phenomena in the host-vector-parasite complex and in the physical environment.

Recent research shows that further development of a mathematical epidemiology in insect-borne diseases must be based on dynamic "time-response" relations between biological systems and factors in the physical environment. The incrimination, efficiency, and distribution of insect vectors have to be determined largely within this concept since individual environmental factors appear to mediate the timing of persistent biological rhythms [4156]. Some physical factors such as radiant energy have been shown to induce phase shifts in cellular rhythmicity [4176]. Furthermore, cyclic activity in lower organisms is manifest both in the free-living [4204] and parasitic states [4225, 4272]. For example, the filarial worm, *Loa loa* (*Filaria diurna*) infests the subcutaneous connective tissue in man in W. Africa but has a daily cycle of appearance in the peripheral blood stream. Efficient vectors in this case are limited to species that attack during the day such as the tabanid *Chrysops dimidiata* [4260]. *Filaria bancrofti* has a reversed cycle in the E. Indies, and is transmitted by insects with nocturnal rhythms of activity such as in certain species of mosquitoes. From the point of view of epidemiology, these relationships are complicated by the fact that they are variable. The periodicity of mosquito activity is mediated and even limited by weather factors[4210] to the extent that peaks of activity for normally nocturnal species are occasionally shifted into the daylight period and those of diurnal species into the night. Moreover, the variability of the rhythm of microfilariae is also well known, *i.e.* the cycle of appearance in peripheral blood vessels is shifted by a full twelve hours in man when the hours of work and rest are reversed [4142]. Variable physiological rhythms, frequently observed in other fields, have led to the suggestion that "biological clocks" operate like imperfect oscillators [4256]. They appear to have an important function in periodic host-parasite relationships [4177, 4211, 4279] and Halberg [4201] suggests that "circadian" rhythms may be "tool and concept" for the physiologist. In future studies on insect-borne disease, the epidemiologist must consider the dynamics of vector development and activity in relation to physical factors at microclimatic, climatic and meterological levels in environmental systems.

Subsect. B. SOME ASPECTS OF BIOCLIMATICS IN INSECTS

1. General Considerations

Physiologically, response in insects to environment is different in many respects to that in man and in other higher animals. Mammals, including man, cannot discern air humidity and, under conditions of high water-vapour pressures and high environmental temperatures which reduce dissipation of heat by evaporation, they experience a discomfort which is related to the state of the central nervous system, to production of body heat, and to deep and superficial body temperature. Insects, on the other hand, react rapidly by *orthokinesis* [1286] to changes in humidity through exterosensory organs. Tsetse flies have humidity perception in their respiratory spiracles which enables them to control respiratory water-loss [4158]. Insects are equally sensitive to air temperature and avoid unfavourable thermal conditions by *klinokinesis* [4286]. Blood-sucking insects are orientated to the host for feeding by a different response known as *klinotaxis*. Insects generally exhibit a higher sensitivity to factors in the physical environment than do higher animals and this is manifest in a highly developed degree of orientation to changes in their surroundings.

2. *Influence of Temperature*

Temperature is a dominant factor in the development, behaviour, reproduction, and survival of insects[4264]. Such parameters as thermal constants, temperature thresholds, optimal and favourable conditions, and lethal levels have been used in the field and in the laboratory as measures of thermal effects in environment [4207, 4273, 4286]. In the laboratory they have been based mainly on static conditions and later work shows that such factors as acclimatization [4139], cyclic variations in rate of exposure [4164, 4242], stage of development [4144], and edaphic factors in the embryonic stage [4148] influence relations between development and temperature. Recent work also indicates that statically derived parameters in laboratory studies are inadequate for predicting development in varying natural habitats [4254]. Thresholds, optima, and constants are satisfactory quantitative measures in describing the development of mosquitoes in natural habitats only when they are related to behaviour and to other factors [4207, 4208]. For this reason, methods based on energy summation [4220] appear to be more adequate in describing the relation between temperature and teneral flight of some insects.

Temperature-velocity curves for development and growth in insects are not considered to be linear[4150, 4168, 4217]; comparison of effects of exposure in variable temperatures with those in constant temperatures should be considered with some reserve [4263]. For example, development at lower thermal levels is more rapid for fluctuating than for constant temperatures [1203, 1254]; but at intermediate temperatures rates correspond more closely to predicted values [1249] and at higher thermal levels growth is retarded [4258].

3. Influence of Humidity

Moisture conditions in insect habitats have an important influence on activity, distribution, and survival[4175]. Transpiration affects water balance, depresses metabolism and retards development in some species [4286]. Resistance to dryness or desiccation is highly correlated with atmospheric moisture [4160, 4219, 4229, 4238]. Most observations on insects in the field have been correlated with mean humidity levels and very little is known about the importance or influence of continuously varying humidities in nature. Low variable humidities stimulate egg production in some insects [4267] whereas females of other species oviposit more freely when humidity is high [4234]. Humidity is highly correlated with flight and dispersal [4169, 4184] and is a limiting factor in the duration of activity in nychthemeral cycling of flight [4210].

4. Influence of Other Factors

Several factors modify the response of insects to temperature and humidity. Light intensity influences the behaviour of some insects [4167, 4172, 4284], and diurnal responses to light may have adaptive advantages for many species [4190, 4280, 4285]. Alternating light and darkness provide an essential cue to the oviposition cycle in *Aedes aegypti* since cyclical behaviour breaks down in both constant light and constant darkness [4188], and since aperiodic behaviour occurs in constant light irrespective of the light conditions during larval upbringing [4197]. Photoperiodism has been shown to influence development [4228] and, with temperature, is a factor in the induction of diapause, a form of arrested development which facilitates survival of the species in certain stages of metamorphosis during unfavourable seasons [4226]. The abundance of some nocturnally active biting flies such as tsetse[4274] and mosquitoes is related to lunar cycles within the fly season. Changes in atmospheric pressure influence activity of mosquitoes either as a direct mechanical effect or indirectly through alteration of atmospheric constituents [4206]. Winds have considerable influence on the activity and orientation of flying insects, especially in dispersal from breeding grounds [4259]. Abundance of many insects such as mosquitoes [4212] and tsetse flies [4161] is related to rainfall or to moist seasons. Some studies tending to show that insects are affected by the electric state of the atmosphere have lead to considerable speculation [4273] (see p. 455).

5. Interdependence of Factors

Some factors such as temperature and humidity interact to a high degree in affecting insect activity, development, and survival. Reproduction and development in some species are influenced differently by temperature and humidity together than by either factor alone [4111]. Humidity affects the temperature preference of some species[4152, 4191] while temperature modifies humidity preferences in other species [4257]. Research workers are not in complete agreement on the parameter that best accommodates the combined effects of these two factors on an insect [1140, 4270]. Wellington [4281, 4283] found that evaporation was a better indication of controlled variations in temperature and humidity on insect behaviour than either of the controlled variables alone. Evaporation power of air is influenced by wind velocity as well as by temperature and relative humidity. Saturation deficit of the air is closely related to transpiration of moisture from some insects in controlled-humidity environments in the laboratory [4159, 4175]; but Leighly [4227] and Thornthwaite [4270] were critical on physical grounds of using saturation deficit as a *direct* measure of evaporation. They point out that evaporation can vary between different natural conditions for a given atmospheric saturation deficit.

Subsect. C. INFLUENCE OF WEATHER AND CLIMATE ON ACTIVITIES AND SURVIVAL OF INSECTS IN RELATION TO DISEASE

Many communicable diseases such as malaria, trypanosomiasis, yellow fever, and filariasis depend on an insect vector for transmission either among humans or between humans and certain other animals that act as reservoir for the parasitic disease organism. The development, behaviour, and survival of the vector is influenced to a high degree by weather and climate. For this reason, endemic and epidemic areas can be geographically defined largely on the basis of climate [4161, 4185, 4223, 4245, 4247, 4266]. Variations in vector activity under fluctuating weather conditions in epidemic areas can influence transmission rate and hence also the behaviour of the disease. In this connection, weather is an important factor in determining the spread and persistence of disease outbreaks.

1. *Influence of Temperature*

Temperature limits the spread and persistence of insect-borne diseases through its influence on the behaviour of the vector and on the development of the infective agent within the vector-host. Seasonal and daily temperature fluctuations under certain conditions limit such vector activities as flight, feeding, and reproduction, all of which are necessary for successful disease transmission among hosts or between reservoir and host. High temperatures reduce the duration and efficiency of flight in relation to time [4210] and also cause sterility in populations [4161]. The biting and feeding of mosquitoes occurs in periods coinciding with or shortly following rising temperatures[4210], and proportions of "gorged" tsetse flies are highest at the end of the dry season when temperatures are high[4253]. The stability of virus level in insect vectors is also related to temperature. For example, the period of loss in concentration of yellow fever virus decreases with temperature following inoculation; virus level remains stable after initial loss at 20° C, but at higher temperatures the rate of gain is a direct function of environmental temperature [4117]. Rate of infection of tsetse flies with trypanosomes is greater at the higher temperatures [4174, 4269], and this agrees with the observation that cyclical transmission among humans in the field is obtained more rarely in cooler seasons [4179]. Longevity, an important factor that limits transmission efficiency in a vector, also depends on temperature [4143].

2. *Influence of Humidity*

Humidity and temperature are largely interdependent in their biological influence on vector-transmission of disease. Activity of tsetse flies is decreased in dry conditions [4276], and humidity, in combination with temperature, determines whether flies are active in open or in shaded areas [4161]. The selection of resting places by mosquitoes, especially in invasion of huts and shelters in Africa, is related to fluctuations in humidity in combination with light and temperature [4216, 4248]. These phenomena might contribute to the variation in sites of infection and epidemics in malaria and yellow fever. Length of the hunger cycle in tsetse flies appears to be closely related to differences in humidity and evaporation [4275], a condition which affects frequency of infection. Survival of many vectors, especially under conditions of starvation, depends on humidity [4145, 4277].

3. *Influence of Precipitation*

When vectors depend on pools, streams, or marshy terrain as a habitat for the development of immature instars, epidemics of communicable disease often show a high correlation with precipitation. In tropical areas, prevalence of disease such as malaria [4271] depends largely on the seasonal abundance of mosquito-breeding places. Precipitation is a major factor in defining the limits of endemic areas for diseases transmitted by mosquitoes and black flies [4149, 4170, 4212, 4235].

4. *Influence of Light and Radiation*

Light and radiation play an important part in the selection of habitats [4239] and in the search for hosts [4161] by insect vectors. Daily migrations of mosquitoes in and out of human habitations are related to light [4248]. These migrations are important features in the diurnal outdoor biting cycles which are primary factors in host-vector and vector-reservoir contact in the transmission of yellow fever and malaria [4192].

5. *Influence of Wind*

Wind has been given little consideration as a factor in transmission of disease by insect vectors; but it affects mosquito activity in at least three ways [4209]. Low velocities stimulate flight and affect orientation in dispersal [4209, 4221], both of which are important factors in the spread of vector-borne diseases. High velocities suppress active orientated flight at ground level [4209] and probably result in "mass transport" for long distances in the upper air [4214, 4284]. Sporadic epidemics in fringe areas of endemic regions may be related to atmospheric circulation and its effect on vector dispersal.

Subsect. D. CLIMATE, DISTRIBUTION AND PREVALENCE OF INSECT-BORNE DISEASES

The distribution and prevalence of epidemic insect-borne diseases depends first on the occurrence and abundance of the vector and secondly on the environmental conditions favourable for the development of the disease organism. The distribution of malaria mosquitoes is determined by favourable temperature [4255] and by the presence of breeding places with adequate rainfall. In some areas the lower thermal limit for development of malarial parasites may be higher than that for the vector and consequently the limit for the geographic distribution of endemic malaria is less extensive than that of the vector. The reverse is known for *Anopheles maculipennis* Mg. and tropical malaria. Suboptimal thermal conditions for the plasmodium cause a high mortality in the vector, and the distribution of tropical malaria either depends on other species for transmission or is limited to the distribution of *A. maculipennis*. Distributions also depend on the regulation of vector activity by various environmental factors such as temperature, humidity, light, and wind. Interdependence of environmental factors, especially temperature and humidity, leads to variations in the incidence of a disease within its geographic distribution. For example, in more northerly countries malaria epidemics occur mainly in warmer years whereas in the south they concur with cool wet weather. This phenomenon is explained by the fact that in the north the plasmodium can develop successfully only during unusually warm years although the vector is always abundant; on the other hand, farther south in environments that are always favourable for the disease organism, mosquitoes are sufficiently abundant for transmitting the plasmodium only when precipitation provides the necessary breeding grounds. Further variations arise in climatic relations when the vector feeds on other animals in addition to man. Periods of drought in India result in severe reductions in populations of cattle, the normal hosts for some species of blood-sucking mosquitoes. During the first rainy season favourable breeding grounds produce rapidly increasing populations of mosquitoes which are forced to concentrate on an alternative host that is usually man. These circumstances lead to fluctuations of the disease in either man or cattle, the alternate hosts [4166].

The distribution of trypanosomiasis in man and in domestic animals in Africa is determined by the climatic and ecoclimatic requirements of the tsetse flies, the trypanosome carriers [4161]. Several species of tsetse are involved and each has definite requirements, especially in relation to temperature and atmospheric humidity. The areas of occurrence of tsetse flies, known as fly-belts, are essentially dependent on the presence of types of vegetation that assure a favourable ecoclimate [4268].

Yellow fever is restricted to hot countries because the causative organism does not develop in the mosquito at temperatures below 20° C. Similarly, filariasis does not occur in Europe beyond latitude 40° N. although suitable carriers are abundant as far as 65° N. and its distribution is limited by the requirement of high temperatures for successful development of *Filaria bancrofti* in the mosquito [4235].

Seasonal variations have been observed within the usual geographic limits of annual distributions of some insect-borne diseases. Under extreme conditions in Africa considerable seasonal movements of tsetse flies occurred between areas defined by certain types of vegetation such as: (*i*) Thicket or forest along water courses; (*ii*) Woodland savannah; (*iii*) Open meadow pan or seasonal swamp, and (*iv*) Forest islands. A high mortality occurred in some types of habitat during seasons of extreme heat and dryness. As a means of survival, populations shifted from one type of habitat to another depending on changes in microclimate. Concentration of flies in small parts of endemic areas not only gave an impression of abundance, but also probably accounted for an extremely localized incidence of the disease at certain times in the season [4162, 4250–4252].

In addition to geopgraphic distribution, a second dimension, vertical distribution, has important implications in insect-borne disease. Some insects are essentially arboreal in their biting habits and others are active at ground level; but these preferences are only relative. Concerning mosquitoes Haddow [1196] states "every species known to the writer may be taken from time to time in the forest canopy and similarly species which frequent that level may be taken in the understorey and at ground level". Seasonal alteration and reversals of the normal vertical distribution may take place in certain species [1173, 1195, 4198, 1237]. Behaviour of insects in these circumstances appears to be related to microclimate; but so far, the complexity of the physical environment has delayed a full explanation of the phenomena. Variation in vertical distribution of vectors is potentially important in the epidemiology of yellow fever in which other animals such as the rhesus monkey [4199, 1200] and marsupials [4278] are suspected to be reservoirs for the disease organism. The rhesus monkey is a canopy-dweller and transmission of the disease organism to man depends on suitable vector contact with both humans and the reservoir. Therefore, the relation between vertical profiles of microclimate and the various vertical distributions of vector activity, and the dependence of disease transmission on the synchronization of biological and environmental rhythms have considerable implications in the distribution of yellow fever and other similar diseases.

Subsect. E. CLIMATE AND ABUNDANCE IN RELATION TO INSECT-BORNE DISEASES

The severity of an epidemic of an insect-borne disease depends primarily on the abundance and density of the vector. This is especially true in malaria if superinfection of the host is an important factor as suggested by MacDonald [1231]. Abundance and density of a vector is influenced by climate and weather in two ways, namely through unusually favourable combinations of climatic factors during the developmental and reproductive periods resulting in high rates of survival and breeding, and through regional and local variations in weather that influence dispersal from widespread breeding grounds with a tendency to localize populations in favourable adult habitats such as river valleys or other sheltered places. When seasons are very favourable, populations of mosquitoes emerge rapidly with a high survival rate. The adult mosquito period may be characterized by a relatively high density and by a relatively short duration, especially if breeding is limited to one generation a year. When seasons are unfavourable, development is slow, emergence is prolonged, and a low density may be maintained over a longer mosquito period. Comparable relations between climatic variations and the abundance and density of tsetse flies reflect fluctuations in the incidence and behaviour of trypanosomiasis [4161]. Climate bears a similar relation to myiasis and the abundance of blowflies [4233]. Weather conditions influence the proportional density and abundance of vectors between breeding places and surrounding areas [4178, 4215]. Climatic factors such as temperature and humidity influence infiltration of anophelines in the upper reaches of estuary creeks in coastal regions of West Africa during certain months of the year, and malaria outbreaks in villages coincide with these invasions [4271]. A survey by Beklemishev [4149] illustrates the effect of climate in limiting the spread and abundance of mosquitoes on a continental scale. He concluded that survival of certain species with a world-wide distribution depended on conditions that allowed at least two generations a year.

Subsect. F. CYCLES IN WEATHER, INSECT-BORNE DISEASES AND METEOROLOGICAL VECTORS

In a broad view of insect-borne disease it is possible to consider that all life is accompanied by an incessant redistribution of material in space and time. Biological rhythms have the function of synchronizing mechanisms of transport at ecological, physiological and biochemical levels of intregration. The appearance of certain biological material or of certain organisms at the right time and at the right place can be visualized as a homeostatic arrangement developing out of the various processes of selection; but the operation of such a system must also be explained by the existence at any particular time of physiological cues. Complex systems in biological organization often produce adaptations that are incompletely optimal or even seriously limited in relation to a particular geographic environment. An understanding of disease outbreaks in these terms might contribute to a more informative estimation of the probability of epidemics. Dissociation of time-cues and endogenous or exogenous rhythms as a result of physiological response to cycles in weather and climate, especially in vectors in an endemic area, would create serious disturbances in ecological systems. These disturbances might conceivably lead from a homeostatic condition to either epidemic outbreaks or extinction of disease.

Seasonal and annual cycles and daily rhythms appear to be a feature of the relation between some insect-borne diseases and the climatological and meteorological environment. The daily rhythm of biting in some species of vectors varies consistently as the insect season progresses[4243]. The developmental cycle of anophelines in studies on Mauritian malaria is relatep to seasonal variation in such environmental factors as temperature[1218]. Bates and Roca-Garacia[1146] recognized the epidemiological implications of biological cycles in jungle yellow fever; but there has been little serious attempt, if any, to integrate biological and meteorological cycling in the epidemiology of disease. However, Rozeboom[1261] has described some important aspects in relation to the alteration of the vector's environment, adaptation to local ecological conditions, and the implication of these factors in controlling vectors effectively with chemical insecticides. The little consideration given so far to biological cycles at the higher levels of integration has merely indicated the complexity of epidemiological systems in a natural environment. Superposition of dynamic influences of climate and weather on biological cycles complicates interpretations further unless environmental cycles can be represented by a few primary factors. Intraspecific variations in some vector cycles create special problems. Mosquitoes occasionally have active and hibernating forms in a single species[1186], or the distribution of a species includes races with different habits in selection of environments and in reproductive behaviour[1183]. These conditions complicate the application of control measures for different environmental conditions in the eradication of certain disease vectors.

Subsect. G. WEATHER AND CLIMATE IN THE CONTROL OF INSECT VECTORS

Disease may be controlled through the suppression or elimination of a vital link in the usual biological cycle. A knowledge of climate and weather and an understanding of their relation to biological systems are fundamental to successful methods of suppressing or eradicating insect-borne disease. Control of insect vectors as the vital link in some diseases may be phenological, ecoclimatic, biological, or artificial. All four methods implicate climate and weather either directly or indirectly.

Phenological control aims at destroying the normal seasonal adjustment in the life-history of the insect and its host. Although this method has been used in agriculture it is not usually suited to medical problems. A special case, however, is the alteration of habitats and prevention of breeding in mosquitoes by regularly altering water levels in impounded waters. This is possible only in irrigation or water-development schemes such as in the Tennesee Valley, U.S.A. in which mosquito populations have been controlled to some extent in the interests of public health.

Ecoclimatic control is designed to alter unfavourably the climatic environment of an organism. This method has been more successful in the control of insect-borne disease. Tsetse flies have been eradicated from some areas in Africa with a corresponding reduction in trypanosomiasis by removing vegetation or altering vegetative growth so that unfavourable microclimates are produced in fly habitats[4161]. Military camps and small settlements in undeveloped subarctic areas of Canada experience a considerable reduction in biting-fly attack following the clearance of surrounding forests that provide breeding grounds and favourable microclimates for sheltering mosquitoes and black flies[4205].

In *biological control* a predatory or parastic species is introduced into the natural ecological system for the purpose of reducing the pest or disease agent. This method depends on a thorough knowledge of meteorological and climatic environments and the selection of species that are capable of adapting to the new conditions. Small species of fish such as *Gambusia* species have been introduced in drainage ditches in marshes to reduce the immature stages of mosquitoes and black flies in New Jersey; but biological control has had few applications so far in insect-borne diseases.

Artificial control generally includes the use of chemical insecticides. The physical and chemical properties and especially the application of insecticides depend on meteorological factors such as temperature and radiation. Chemical properties of many insecticides break down or are modified when applied in certain environments. Toxicity of stomach poisons, fumigants, and contact insecticides, for example, is influenced by environmental temperature[4153, 4155] and probably also by other physical factors that alter metabolism and activity in insects. Since weather influences the activity and physiological responses in insects, space sprays, aerosols, and contact insecticides may be biologically ineffective unless treatments accord with the weather conditions that are known to promote maximum contact and high toxicity[4265]. Space sprays and aerosols are most effective against mosquitoes when application coincides with meteorological conditions that promote a high level of flight activity in populations.

Climatology and its relation to problems in insect-borne diseases have been largely descriptive. Future research must reflect a grounding in physics and a higher level of integration of both meteorological and biological systems if a fuller understanding of the role of insect vectors in disease is to be achieved. Landsberg[4224] has speculated that the greatest advances of climatology are destined to lie in the border field of biology provided cooperative research becomes the trend in attacking future problems. The recent reawakening of interest in medical biometeorology[4232] will undoubtedly lead to more extensive studies of ecological aspects of disease. In the case of insect-borne diseases, progress will be marked, among other aspects, by the design of long-range experiments with sufficient physical and statistical validation to quantitatively distinguish the relation between environmental and vector cycles in epidemiology.

Section 4. Hibernation and Reproduction of Animals

by

G. E. FOLK, JR.

Subsect. A. HIBERNATION

1. Introduction

The understanding of hibernation has challenged biologists since the time of Aristotle[1289]. Field biologists in many parts of the world have been perplexed by this adaptive mechanism; perhaps as they find tightly-curled hamsters under cold winter rocks in the mountains of Rumania; or upon observing dormant pocket-mice on a cool midsummer morning in the Sierra Navada; or upon watching an Oregon ground squirrel digging himself out of ground that had been frozen for 8 months; perhaps as they observe that captive spiny mice of Norway in the morning become as stiff and quiet as in death; or as the field worker above the Arctic Circle of the European area digs out a dormant winter colony of vipers or lizards from beneath a mass of grass roots. All of these dormant animals have at times been considered winter-killed by some observers, only to see the animal lifting a drowsy head as it awakens. The question asked about this phenomenon in this section is what relationship exists between weather, climate, and the hibernation. Of the climatic factors of light, moisture, wind and temperature, most of our attention must be given to the presence or absence of a cold season or an arid location. The first question must be: Is hibernation a common physiological response? The second: How does this response compare with other mechanisms for combating environmental extremes? The discussion of the occurrence of hibernation requires a review of the classification of types of temperature control (see pp. 208).

Homoiothermic and poikilothermic animals

The animal kingdom is divided into two groups: (*i*) The *homoiotherms*, consisting of birds and mammals which maintain a relatively constant body temperature, and (*ii*) The *poikilotherms*, which take on the temperature of the air, conducting medium, or radiant environment around them (invertebrates, fish, amphibians, reptiles). We may state that hibernation occurs in both groups of animals, if we accept for the moment that this phenomenon consists of resting in a dormant state in close quarters throughout a specific season.

How do animals combat environmental extremes?

The environmental extremes of heat, cold, and aridity require numerous adjustments from animals in the two groups mentioned. To survive during a period of cold, all poikilotherms make use of hibernation. The mammals and birds are less apt to resort to this drastic physiological change, and instead they will raise their metabolism[4302], or increase their insulation[4303], or maintain very cold extremities or a cold skin[4306]. To permit survival in heat, evaporative cooling takes place from panting or sweating; vasodilation of the skin occurs, and acclimatization is conspicuous as water conservation and circulatory responses are made more efficient. Most importantly, small homoiotherms and all the poikilotherms avoid the extreme environment where possible by being nocturnal or fossorial, and by moving rapidly from the coolest possible spot through the heated area to another cool spot. The challenge of lack of water is handled in a variety of ways. Many animals can form metabolic water from dry food. The small animals remain in the coolest confined location where the vapor pressure is higher than outside. Large animals sometimes permit their body temperature to rise and then dissipate the stored heat during the night. In place of these defenses against heat and aridity, the response of invertebrates and reptiles is apt to be dormancy; some mammals and birds also become dormant in the desert. This phenomenon has been called *aestivation,* but it has now been shown to be so closely allied in a physiological sense to hibernation that it is not necessary to separate the two[4290, 4291]. We must now consider in more detail the types of hibernation experienced by invertebrates, amphibians, and reptiles compared with that of mammals and birds.

What is hibernation?

Mammalian and avian hibernation is a state of dormancy associated with reduced heart rate, respiration, body temperature, and total metabolism. Dormancy means cessation of coordinated locomotor movements. The body temperature remains about 1° C above environmental temperature and the animal usually awakens if cooled to a critical level, which is about 1° C. The only consistent changes found in the blood are an increased production of heparin[4301] and a rise in serum magnesium[4312]. This form of hibernation is distinct from that of poikilotherms in that the mammal and bird can awaken from dormancy voluntarily. Because of this distinction it is useful to borrow terms from another area and speak of *obligatory hibernation* applying to poikilotherms and *voluntary hibernation* applying to mammals and birds. The importance of the term "obligatory" is made clear as we realize that the resistance to cold of reptiles, for example, depends upon their ingenuity in selecting an area of earth or vegetation that will stay above a critical temperature level in the winter; most importantly, this area must warm up at the appropriate time and release them from their cold micro-climate. The ingenuity used in finding these areas is shown by the distribution of reptiles in Europe as far north as the Arctic Circle[4294]. It is not only the reptiles as a group which are restricted by appropriate terrain in this fashion. Within the mammal group the cave bats are wellknown voluntary hibernators and the northernmost distribution of these animals in winter depends also on their finding an appropriate hibernating area of natural type which will not be below the critical temperature in winter (about 2–6° C)[4298]. This restriction also applies to hibernating birds[4293]. The other mammalian hibernators have more flexibility since they can build or alter their private micro-climates.

2. *Geographical Distribution of Animals and Hibernation*

Hibernation appears to be a physiological adaptation of populations of animals in hot, arid, and cold areas. Discussing the cold areas first, we now ask just how necessary a mechanism it is. We will consider only mammalian hibernators; these are all the size of marmots or smaller. There are about twenty-three non-migrant mammals of this size which inhabit the northern third of Canada; only *four* of these hibernate[4295]. Another test can be applied as follows: There are eight non-migratory mammals which have a distribution covering most of the United States and Canada; only *two* of these are hibernators[4295]. This survey indicates that mammals combat an extreme environment by turning to a well-filled "bag of tricks." The beaver uses engineering skill to keep his environment safe during the winter. The red squirrel raises his metabolism[4314]. Only a few of the mammals resort to voluntary hibernation.

The small number of hibernators compared to the total number of mammals with the same distribution shows that the ability to become dormant probably does not play a role in governing the distribution of mammals. The broad distribution of several hibernators of the same species over a large number of climatic areas is evidence that often large populations of the species do not make use of their physiological ability. The two hibernators which have a range over most of the U.S. and Canada are the meadow jumping mouse and the deer mouse[4311]. Another illustration is the 13-lined

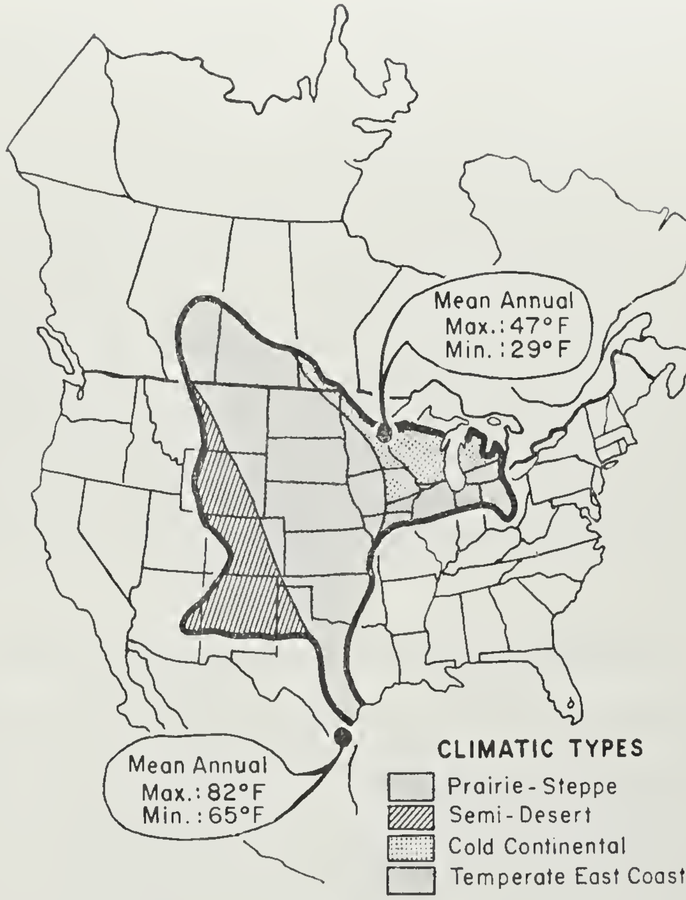

Fig. 99.
Distribution of the squirrel (*Citellus tridecemlineatus*) over N. America, showing four climatic types within its range; the species must have a very different "winter-physiology" in the northern and southern areas.

ground squirrel which is found from the Gulf of Mexico to the middle of Canada (Fig. 99). Four climatic areas are included within this range. Hibernation is important in the ecology of this animal in the north, the dormancy or aestivation is important in the south, and in the middle part of the range the species probably maintains a constant body temperature most of the year. These three species (13-lined ground squirrel, meadow jumping mouse, and deer mouse) would be referred to by Darlington as "dominant species" showing general adaptation which makes them superior to others in many different climatic areas[4296]. These relationships between climate, geography, and physiological mechanisms are complicated. Bartholomew has clarified the picture by his evidence that physiology helps to explain how mammals can live where they do, but it rarely explains the exact limits of their distribution[4305]. This idea is not immediately apparent. For example, it is known that the manatee is unable to survive cold water[4314], and the fur seal is unable to survive warm water or hot air[4292]. It would appear that the distributional control of these species is physiological. However, as Bartholomew points out, "In the case of desert animals, the heat and aridity may actually limit the occurrence of these species but the desert comprises only part of the perimeter of their ranges. On other parts of the perimeters, different factors must be limiting"[4305]. Presumably some of these factors, other than physiological resistance, would be competition, habitat selection, diet, and behavioral mechanisms. The ability to hibernate does not appear to be a distributional determinant.

3. A Theory of Hibernation (Mammalian and Avian)

The relationship between animal distribution and hibernation has been considered; in order to go into more detail (for example, to relate weather and the onset of dormancy), it is necessary now to discuss the physiological syndrome which results in hibernation. Several theories of hibernation have been proposed[4308, 4309]; that of Morrison[4310] is proving the most useful A comparison must be made with the response to cold of ordinary mammals and birds. Consider the over-simplified example of white rats exposed to cold as the only environmental change. The cold-response will be an increase in metabolism over resting level and occasionally an increase in insulation [4302, 4303]. The usual body temperature is maintained. Morrison's theory states that under some circumstances the animal may draw upon the mechanism of hibernation by "turning off" the cold-response just described for combating cold. If the animal is the size of a marmot or smaller, and if the air temperature is relatively cool, and if it remains resting, then its body temperature will drop steadily. If the animal is larger than the marmot (for example, the size of the raccoon and bear), the circumstances may be the same but the drop in body temperature will not occur. Apparently this hibernation response can be turned on at any time of the day or the night or the year. Two mammals have now been studied in which the *resting* animal usually has a temperature which is directly proportional to the air temperature: the bat and the birch mouse[4304, 4307]. This could be called daily-hibernation or day-hibernation. This observation and the occurrence of cases of semi-dormancy demonstrate that hibernation is not necessarily a cold-climate phenomenon. This day-hibernation is common in the pocket-mouse[4291], infrequent in the 13-lined ground squirrel, and rare in the golden hamster. The potential state can be converted to deep hibernation quite readily, except in the case of the golden hamster. This means that in midsummer in warm climates, hibernators can be placed in a cold environment, and they may become dormant. If this hibernation is prolonged, it may prove fatal, because a certain amount of preparation for deep hibernation is obvious under natural field circumstances.

4. *Preparation for Hibernation*

The most conspicuous effect of weather and climate upon some species of hibernators is found in the preparation process. The adjustment to changes in temperature of some species is influenced by changing hours of daylight [4302]. Temperature, humidity, and change of diet must also be important. The response is usually one of fat storage, or in the case of hamsters, the storing of enormous amounts of food. The amount of conditioning by cold exposure required before hibernation varies with the individual animal and with the species. As winter progresses periods of dormancy become longer[4299]. Acclimatization to cold does occur with hibernators[4288, 4313]. As yet the relationship between this response and the process of going into deep hibernation has not been analyzed. In our colony of 13-lined ground squirrels maintained in an unchanging light cycle for three years, we have found that some individuals will go into hibernation in 24 hours after being changed from a warm constant-temperature room to a cold room*. Yet acclimatization to cold takes at least seven days in the ground squirrel and hamster[4297]. Probably part of the explanation of the apparent lack of dependence upon climatic preparation is the presence of the internal rhythm. There is an annual chain of events throughout the process of hibernation, mating, raising young, and putting on fat for the winter. This internal rhythm undoubtedly runs its course, governed and clued and supplemented by factors of the external environment. For three years we have observed evidence of this internal rhythm in the spring season at the other end of the annual cycle of events. Our ground squirrels were in intermittent hibernation for four months each winter[4300]. Toward the end of each winter some regular hibernators refused to go into the dormant state. There was no known clue from the external environment. Undoubtedly the internal rhythm called for cessation of the lazy period of the cold winter-vacation. This laboratory model of ground squirrel hibernation can be matched by similar observations in the field.

* These environmental chambers were built and many experiments were conducted there with the support of the U.S. National Science Foundation.

5. *Advantages of Hibernation*

Hibernation and aestivation have been presented as the same physiological phenomenon. This means that the body temperatures of some hibernators will passively follow ambient temperature from 2–20° C without eliciting arousal. What is the advantage of this state to these animals? Some small mammals and birds, because of high metabolic rates, are faced with an acute need for a continually available supply of food. An ability to lower their metabolism drastically conserves the food supply. The medium-sized hibernators, such as ground squirrels and marmots, make use of this ability on a seasonal basis, not a daily basis. Experimental proof has been obtained by Bartholomew who found that dormant pocket mice actually lost less weight than their non-dormant controls[4291]. He also showed for birds that a torpid poor-will could survive for at least 100 days on the energy derived from 10 g of fat[4293]. Some naturalists believe that dormancy may prolong the life of mammalian hibernators. For evidence, the unusually long life of cave bats (21 years) is cited.

To summarize, it is clear that either obligatory or voluntary hibernation is found in many, if not most, climatic areas. The phenomenon seems to be a modification of ordinary physiological regulation, and there is little reason to make a distinction between hibernation and aestivation.

Subsect. B. REPRODUCTION

The reproductive function in animals can almost be said to be as variable as there are species of animals. The biology of each animal provides a varied story because each of the following components, if present at all, may be totally unlike from species to species: (*i*) Migration for breeding; (*ii*) Growth of secondary sexual characteristics; (*iii*) Courtship; (*iv*) Coming into heat, rut, sexual receptivity, or sexual activity; (*v*) The fertilizing process; (*vi*) Pregnancy; (*viii*) Parturition; (*viii*) Care of young, and (*ix*) Involution of the reproductive tract.

The present chapter is concerned with discussing the possible influence of weather and climate upon the factors just listed (see also p. 571). The degree of this influence is frequently unknown and untold combinations of reproductive responses and climatic factors remain for study in the future. Only a few examples of distinctly different expressions of the "reproductive formula" will be described. Some principles and observations relating to reproductive biology will be considered, likely environmental factors suitable for acting as "influences" will be listed, and known cases of environmental control will be described. Some of the examples have been selected from Marshall's *Physiology of Reproduction*[1328].

1. *Observed Phenomena of Reproductive Biology*

(1) Animals can be classified into two types by their reproductive behavior: *continuous breeders and seasonal breeders*. Examples of continuous breeders are some primates including man and some domestic species including chickens, horses, cows, rabbits, and laboratory rats and mice. The seasonal breeders include some domestic animals like most breeds of sheep and most wild animals in the free environment.

(2) The *periodicity in breeding* is obliterated in some tropical climates where there is little variation in temperature throughout the year. This particularly applies to land mollusks, one species of toad, insects, and marine invertebrates[1333]. In the case of an Andean sparrow, the species may nest in all months of the year but each individual adult male has a testis cycle of 6 months' duration[1330]. According to Metten[1329] the common dogfish has no breeding season; it is always sexually active.

(3) As a generalization, a *breeding migration is almost universal in the fish group*. The process of growth and the process of reproduction are alternated. As a result the fish are in poor condition when spawning takes place. In some cases the fish has been for long months in aestivation or hibernation and the reproductive cells mature during that period. After spawning, feeding and growth begin again. In contrast, mammals after hibernation appear to be in good condition for immediate breeding.

(4) It is characteristic of the *amphibian* that the ova develop during the winter hibernation when the animals eat little or nothing. The testes of the males also increase enormously in size with the approach of the breeding season. For this group, however, Moore[1331] states there are no features common to the group which suggest the appropriate controlling influences. Spermatogenesis may be rapid during midsummer, or continuous throughout the year, or it may occur slowly during summer and winter.

(5) *Reptiles* that hibernate usually begin to breed shortly after the termination of the hibernating period as do some fish and amphibians. The rule for reptiles as with most amphibians is that breeding occurs only in response to certain external stimuli. Of these, temperature is the main factor[1328]. Nevertheless, there are differences due to classification; for example, there are two species of large reptiles (Caimans) inhabiting the Amazon: one breeds in October and November and the other in May and June.

(6) Special mechanisms have been developed in reptiles concerned with

the *retention of the eggs for development within the mother.* This internal development has been evolved where situations of cold or desiccation would prevent the development from occurring efficiently outside the body. Internal development is found in lizards above 4,000 ft. and in deserts of Australia.

(7) In summing up these observations, one generalization is warranted: there are *two classes of animals,* one of which is in poor condition before and after breeding (migrant fish, amphibians, fur seals)[4317], and another which is in an extraordinarily high state of development (many birds, male deer some fish; see also ground squirrel discussed below). In the poor-condition group it is almost as if there were two animals: for a while the vegetative animal exists, and then, in some instances influenced by climatic factors, the reproductive animal takes over. This especially applies to some migratory fish and to insects which have a long larval life.

2. *Possible Controlling Factors*

The following list of internal and external influences upon reproduction have been suggested as being important in the life history of some groups of animals, starting with protozoa: (*i*) The internal rhythm; (*ii*) The state of nutrition and quality of food; (*iii*) Phases of the moon; (*iv*) Temperature; (*v*) Salinity; (*vi*) Period of inundation; (*vii*) Rain which releases animals from mud or raises atmospheric humidity; (*viii*) Light; (*ix*) Temperature and rain combined; (*x*) Crowding of populations or individuals; (*xi*) Cycles of different kinds of external stimulii, and (*xii*) Special local or ecological stimuli (such as the existence of appropriate nesting sites).

3. *Known Control by Weather and Climate*

The influence of weather and climate upon reproductive processes is frequently difficult to determine. There are variations in the breeding process for reasons not at all apparent, and frequently no correlation with climatological data can be obtained. In many cases, there is a regular time of day or month or year for the breeding process, but the factors which bring about this regularity have not been analyzed. Results from laboratory climatic-chambers must be interpreted cautiously, because in some cases laboratory-kept animals and field-kept animals yield different results[1325]. It is easy to forget that single-factor laboratory experiments may not apply to the animal in the free environment, but frequently there are no other data available.

The internal reproductive rhythm

It is essential that the student understand the internal rhythm from the start. It consists of a chain of physiological sequences, comparable in part to the chain-behavior-patterns of insects and birds. In a few species there is probably no external control at all, but only an internal reproductive rhythm. These cases are represented by the most extreme types of continuous breeders in the free environment. Also seasonal breeders which breed in different months each year in rotation demonstrate an internal rhythm, such as the sooty tern which has a breeding season every 9 months[4327]. The complexity of the types of climatic influences upon the internal rhythm is indicated by the observation of Marshall[4328] concerning amphibians which he studied: "There appears to be abundant evidence that breeding in mature amphibians does not occur only cyclically but takes place only in response to certain definite external stimuli which are of different kinds and in a state of nature occur naturally in a regular order". The presence of external stimuli of different kinds occurring in a regular order help to explain why many animals have variable breeding activities from year to year.

Temperature change

Some examples of known control by individual factors will now be considered in cases where experiments have apparently been carried out. A change in *temperature* controls the dividing of certain protozoa, the two breeding seasons of sponges, the limits of the breeding season of Nemertean worms, the sexual development of flat worms (especially a lowering of temperature), the production of winter eggs of Rotifers which require fertilizing before they can develop, the development of male plant lice that fertilize eggs which can tolerate cold, and the egg-laying by nudibranchs and oysters *(Ostrea virginica)*. Some fish show extreme sensitivity to changes of temperature and only spawn at certain temperature levels, which may be as far apart as 3.5° C and 20° C for different species. A common English frog *(Rana temporaria)* varies its spawning time with temperature; and according to Marshall[4328], in reptiles, temperature is the main factor which controls breeding.

Cold

The influence of the single factor of cold-exposure on the female white rat is to lengthen the duration of the estrous cycle by a longer proestrus and estrus[4319]. When the experiment was repeated on female hamsters maintained in cold for 90 days, they went into anestrus[4322]. During the last 10 days of cold exposure there was partial cold adaptation of sexual function. Senile male hamsters in the cold showed gonadal atrophy, but this was found in only a few (37%) of the warm room controls[1323].

In the ground squirrel cold weather brings about hibernation. Foster *et al.*[1321] implied that gonadal inactivity is necessary before cold can induce hibernation. Wells and Zalesky[4335] also found a relationship with cold exposure. Their ground squirrels showed spermatogenesis under varied lighting conditions only if the ambient temperature was sufficiently low. In the ground squirrel colony studied by Landau[1326], in midwinter the testes of warm-room males become scrotal, and these animals if placed in the cold did not hibernate until the testes became abdominal again. However, in another colony[1320], at the end of four months of hibernation not only were the ground squirrels in an excellent, fat condition, but the mean weight of the testes of warm room controls was only 23% of the mean weight of those of the hibernators. This illustrates the rule that the 13-lined ground squirrel leaves hibernation prepared for breeding.

Phases of the moon

Both migration and sexual activity of the following animal groups are influenced by phases of the moon: some annelid worms, sea-urchins, mollusks (scallops and pearl oysters), and some insects.

The influence of wet and dry seasons

The control of breeding of mollusks, particularly the land snails, is controlled by wet and dry seasons, as would be suspected. The control of spawning in the crossopterygians *(Polypterus)* of several species is determined by the period of inundation of the rivers; in the dipnoan of Australia the exact time of breeding varies from year to year depending upon when the swamps are wet by rains; in a careful series of laboratory experiments, Bles[4318] showed that the breeding of Zenopus, the African frog, depends upon a temperature rise plus rain.

Light

Some experimental animals kept in complete darkness or blinded, show estrus at the same season as control animals kept under normal light conditions. Yet light has a well-known role in hastening the onset of breeding seasons. This control function must be related to synchronizing reproductive events in all members of a local population, causing them to be in similar reproductive states at the same time.

The control over reproduction in some amphibians of northern latitudes, once they have emerged from their winter retreats, has been shown experimentally to be controlled by hours of daylight[4328]. The male lizard *(Xantusia)* has a testicular cycle regulated (a) by day length and (b) by temperature[4316].

In mammals a frequent example cited is the experimental work of Yeates[1337] who demonstrated that one could hasten the onset of breeding in sheep by decreasing the hours of daylight. These experiments also illustrate the frequent difficulty in reconciling field and laboratory data, since a survey of a large sample of sheep "in the field" showed an onset of heat on July 8 one year but Sept. 1 another year. No significant correlation with meteorological data was found to explain the difference in the two years[1332].

The control by light over breeding seasons in birds has received particular attention. This is not the only factor of control because at times when tropical birds are imported they maintain their original breeding rhythm. Some birds will not breed at all if the appropriate factor, such as rain, is missing. Many birds are photoperiodic; the variable response may be the time of reaching sexual maturity, or the time of egg laying[1331]. Recent experiments by Wolfson[1336] have shown that it is the period of light and not the period of darkness which determines the response. Probably there are different degrees of response to the photoperiods, which summate. The evidence for the physiological pathways of the photoperiodic response has been reviewed by Hendricks[1324] and Nalbandov[1332].

To summarize the varied concepts discussed in this section, it is useful to apply to all animals this statement of Marshall: "The reproduction of insects depends among other things upon the nature of the diet, the chemical conditions of the surrounding media, upon the moisture of the air, and upon other circumstances which are often unknown."[1328]

Survival value of climatic influences

Some teleological reasoning as to the purpose of climatic control is justified. Some writers state that a restricted breeding season has evolved due to its increased survival value to the off-spring. A classic example cited is the nesting of giant emperor penguins in the dark season so that the young birds may have the entire summer to be fostered by their parents; as another example, an insect midge has an optimum time of emergence which coincides with an appropriate stage of growth by the food plant. The control of light upon both of these breeding cycles is important to "clue" the seasonal timing which is already fairly exact due to an internal rhythm. This fairly exact internal timing of seasonal breeders is sometimes found even where environmental conditions are uniform throughout the year, showing climatic clues are not always needed[1315]. However, the usual effect of the removal of climatic influences, as in domestic species[1332], is the release of the genetic potential for prolonged breeding seasons so that some species then become continuous breeders.

PART VI

The Microclimate of Space Vehicles
(An Introduction to Space Medicine)

by

DONALD R. EKBERG

Section 1. From Earth to Space

As man proceeds away from the surface of the earth, a number of environmental parameters are altered. Of these parameters *pressure, temperature, radiation,* and *gravity* may be considered of major importance. These four variables are depicted graphically in the Figs. 100 and 101.

Pressure

Taking one atmosphere (760 mm Hg) as the average pressure at sea level, it may be seen that the pressure drops off fairly rapidly within the troposphere, and then slowly throughout the stratosphere and ionosphere. At 18,000 ft. the pressure is one-half that at sea level, one-quarter at 34,000 ft , and one-eighth at 48,000 ft. At 150,000 ft. the pressure has dropped to approximately 1 mm Hg. Up to 100,000 ft. the percentage of dry gases within the atmosphere is relatively constant. Water vapor ranges in amount from 1–5% throughout the troposphere. However, above the troposphere the amount of water vapor is neglibible.

Temperature

In the United States the standard temperature at sea level is taken as 15° C. Unlike pressure, the temperature falls off linearly up to an altitude of approximately 35,000 ft. This decrease is 2° C/1,000 ft. increase in altitude. Thus, at 35,000 ft. the average temperature is —55° C. From 35,000–100,000 ft. temperature is isothermal and above this altitude the temperature varies as shown in Fig. 100. At extreme altitudes the high temperatures given refer to the kinetic temperature of the gas molecules, which is proportional to the mean square of the particle velocity. Any object maintained at these high altitudes would receive negligible heat from the gas molecules due to the rarefied state of the gas. The temperature of the object would be determined almost solely by radiation.

Radiation

The word radiation covers quite a bit of ground—one may consider the electronic spectrum 0 c/s all the way up to cosmic rays of 10^{22} c/s or greater. However, if we neglect the lower part of the spectrum (DC to infra-red), we are left with a frequency range of 10^{13}–10^{22} c/s. Within this range we may now consider ionizing radiations; infrared, visible, and ultraviolet radiation, discussed on p. 338–340. Of the ionizing types of radiation, those of particular interest to a person venturing away from the earth are the particulate ones, cosmic and Van Allen (see Figs. 100 and 101).

The primary cosmic rays arriving in the vicinity of the earth from outer space are known to be atomic nuclei, atoms stripped of all their planetary electrons. Their incident directions would be isotropically distributed in space if it were not for the magnetic fields produced by the earth and the sun. The magnetic field associated with sun-spot activity results in an appreciable decrease in the number of particles with energies up to about 1 BeV (billion electron volts), and the earth's magnetic field produces the well known latitude effect and the east-west asymmetry (see Fig. 100).

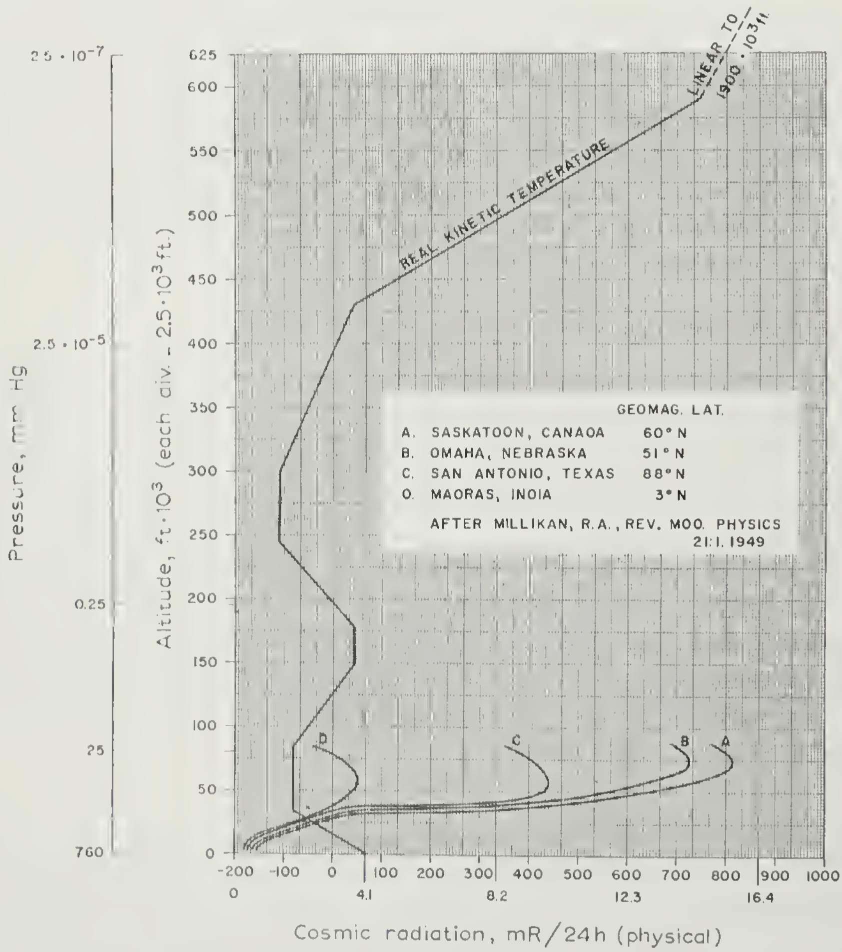

Fig. 100.

Variation of pressure, temperature and cosmic radiation with altitude. The abscissa contains two scales: the upper scale is the temperature in °F; the lower scale is the cosmic radiation in milliroentgens. A: Saskatoon (Canada), geomagn. lat. 60°N; B: Omaha, Nebr., geomagn. lat. 51°N; C: San Antonio, Tex., geomagn. lat. 88°N; D: Madras (India), geomagn. lat. 3°N (after Millikan, *Rev. mod. Phys.*, *21*, 1 (1949).

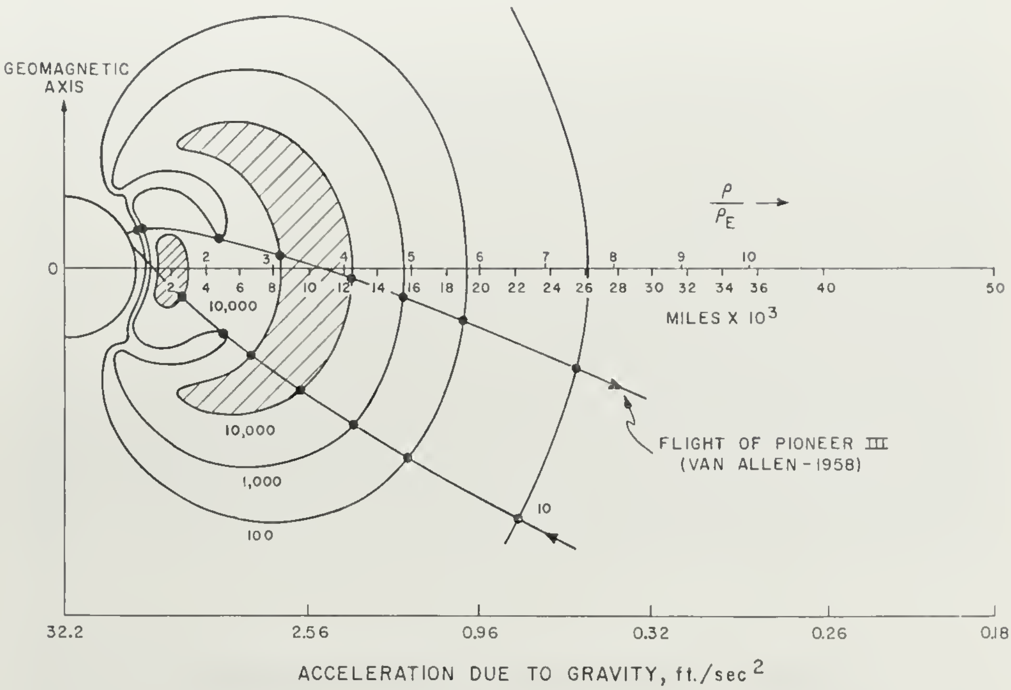

Fig. 101.
Variation of the Van Allen radiation (see p. 23) and gravity with altitude.

$$\frac{\rho}{\rho_E} = \frac{\text{distance}}{\text{radius of the earth}}$$

Outside the earth's magnetic field the composition of primary cosmics is about 90% protons, 8% alpha particles, and 2% nucleons of atomic number greater than 2. The primary cosmics striking the top of the earth's atmosphere are about 80% protons, 19% alpha-particles, and 1% heavy particles. As these particles enter the atmosphere they interact with various gas molecules and produce particulate and non-particulate forms of radiation.

Van Allen *et al.*[4378] have described a high intensity particulate radiation, which appears to be trapped within the magnetic field of the earth. This radiation (herein termed Van Allen Radiation) is distributed about the earth like two doughnuts (see Fig. 101). The inner radiation belt is composed primarily of protons, while the outer belt is composed primarily of electrons. These belts do not appear to be constant in size or intensity, for they vary at the time of solar flares. Further study is being considered in order to delineate these zones of radiation with respect to size, particle intensity, and spatial distribution.

Gravity

An object must be placed a considerable distance away from the surface of the earth before the force of gravity becomes negligible; for this force is inversely proportional to the square of the distance from the center of the earth (see Fig. 101). At 4,000 miles from the earth's surface the force of gravity is one-fourth that at sea level, at 8,000 miles one-ninth, and so on. An object which is placed into orbit must have a centrifugal force equal and opposite to the force of gravity at that altitude. Hence, the gravitational and centrifugal forces on the object are in equilibrium. Physiological effects of this weightlessness will be discussed in a later section.

Numerous studies have been made of the effects on man and other animals of forces greater than one *g* (for gravity: 32.2 ft./sec^2). Such forces ranging over 10 *g* will undoubtedly be encountered by vehicles leaving and returning to the earth, but not during orbital or interplanetary free flight and, hence, will not be considered in this Part.

Section 2. The Physiological Requirements of Man

As has been shown in the first section the physical environment away from the surface of the earth does not meet with the comfort and/or vital requirements of man. There is essentially no pressure, ionizing types of radiation are indeed hazardous, the temperature will vary considerably depending on the orientation to the earth and sun, and gravity is, for all intents and purposes, non-existent.

In order to devise a system for the protection of man in this strange environment, it is first necessary to review the requirements of man for comfortable existence.

1. Pressure

Living tissue is probably unaffected by pressure *per se*, except at very high pressures[4358] where the gel-sol relationships of cells are affected. Tissues as well as whole organisms will equilibrate with an external pressure over a wide range. However, rapid changes in pressure will prove deleterious to an organism such as man[4357, 4379], *i.e.* equilibration takes time.

Of prime importance in a consideration of pressure is the partial pressures of the various gases in the environment, since this is a prime variable in determining their concentration in tissues.

Oxygen

If we accept 90% saturation of the blood with oxygen as a minimal level for long periods it may be demonstrated that this degree of saturation corresponds to an alveolar oxygen partial pressure of about 60 mm Hg. Conversely, Mullinax and Beischer[4359] consider 425 mm Hg as the maximum partial pressure of oxygen that may be breathed indefinitely. Thus, we may take 147 mm Hg pressure, if 100% oxygen is breathed, as the minimum total pressure allowable, for the alveolar carbon dioxide pressure is 40 mm Hg and the alveolar H_2O pressure is 47 mm Hg. If a diluent gas such as nitrogen is utilized the minimum total pressure would increase with the amount of nitrogen introduced. However, it should be emphasized that at this total pressure (equivalent to an altitude of 39,000 ft.) there is a possibility of seroembolism formation if the body is not thoroughly denitrogenated. Since it has been shown[4349] that the bends are rarely developed below a pressure equivalent to 25,000 ft. altitude (282 mm Hg), it would seem advisable to accept this pressure as the minimum.

Carbon dioxide

Numerous reports have been written concerning the maximum allowable concentration of CO_2 ([see refs. 4345, 4348, 4364]). Three percent carbon dioxide in some cases[4352] has produced no ill effects. Yet Otis and Chapman (in 1951) developed a definite decrease in their sensitivity to carbon dioxide as judged by their rate of ventilation and alveolar carbon dioxide partial pressure. Becker and Clamann[4341] could find no pathological changes following a three day exposure to one percent carbon dioxide. Thus, it would seem advisable to establish 8 mm Hg as the maximum allowable carbon dioxide pressure for long term flights.

Nitrogen

Very high pressures of this gas will produce "nitrogen narcosis" (extreme *euphoria*). Obviously very high pressures of nitrogen will not be considered in any space vehicle carrying man. Thus, we may consider nitrogen as only a diluent gas. In fact, it may not be necessary to consider nitrogen as a necessary environmental constituent except to reduce the fire hazard, or possibly to reduce the occurrence of *atelectasis* (*i.e.* the nonexpansion of the lungs)[4365a].

Water vapor

The partial pressure of water may be taken as 10 ± 5 mm Hg[4379b]. This p_{H_2O} range will maintain comfort over a wide temperature range.

Total pressure

In view of the required levels of the above mentioned gases, the total pressure may vary from 1/3 to 1 atm. If it is necessary to construct a vehicle of minimum weight, attention must be paid not only to physiological factors such as dysbarism and atelectasis, but to engineering considerations as well. These include such things as blower power requirements, leak rates, container weights, etc.

2. *Temperature*

Man has the ability to withstand rather extreme temperatures for short periods of time[1372]. However, for long term exposure it is advisable to maintain him within the comfort zone. This zone depends on a number of factors: humidity, air velocity, activity, atmospheric pressure, the amount of clothing being worn, etc. For a thorough discussion of these factors the reader is referred to pp. 426–436 and to the work of Winslow and Herrington[1382], Selle[1368] and Webb[1379a].

3. *Radiation*

At the present time in the United States the yearly maximum permissible exposure is given as 5.0 rem, with an emergency exposure limit of 25 rem (Atomic Energy Commission). One rem is that amount of any radiation required to produce the same degree of biological effect as 1 roentgen of hard X or gamma radiation. One rem is also equal to the product of rad (radiation absorbed dose; in 100 ergs/g of tissue) and RBE (relative biological effectiveness). For densely ionizing particles such as alpha particles the RBE is much higher than for less densely ionizing particles such as electrons. RBE is roughly equivalent to LET [linear energy transfer, in KeV (= 1000 electron volts)/U of tissue]. Thus, for the particles of cosmic and Van Allen radiation the effect may be expected to be greater than the dose measured in rads or roentgens. At the present time, the rem dosages of cosmic and Van Allen have not been measured, only estimated. Tobias[1373] estimates the RBE of primary cosmics to be about 7. The RBE for Van Allen radiation may be less than 2 for protons (due to their very high energy), and probably only about 1 for electrons.

4. *Gravity*

Very little is known concerning the effects of weightlessness (see p. 651). Thus, we may only speculate as to its long term effects from our knowledge of short term (up to 5 minutes) effects. Unfortunately the Russian data are not available, but they report no ill effects to man during or following a flight of one orbit. Normally, orientation information with respect to the immediate environment is presented to an individual from three sources: (*i*) Proprioceptors; (*ii*) The vestibular apparatus, and (*iii*) Visual cues. If an individual is placed in a weightless environment, the first two mentioned are of value only when the individual moves because they are both gravity dependent. Thus, one must adapt to this peculiar situation on visual cues alone. Feeding may also prove to be a problem, since food must be introduced past the pillars—area of tonsils—so that it may be swallowed. Movement in such an environment will also have to be learned. Long term weightlessness may produce effects similar to those produced by prolonged immobilization, *i.e.*, bone demineralization, muscle atrophy, etc.

5. *Metabolism*

If we consider a 2.0 m^2 (80 kg, 180 cm) man and assume an average metabolic rate somewhat greater than basal of 50 kcal/m^2/h, we have a man producing 100 kcal/h or 2400 kcal/day. Furthermore, if we assume a respiratory quotient of 0.85, the caloric equivalent of one liter of oxygen is 4.8 kcal. Thus, we calculate the oxygen consumption to be $\frac{100}{4.8} = 20.8$ l/h or 500 l/day and the carbon dioxide production is 17.7 l/h or 425 l/day.

In order to maintain this "machine", it must be given adequate food to metabolize at least 2400 kcal/day, of approximately the following composition: 52% carbohydrate, 33% fat, and 15% protein. This diet composition has been arrived at by Sargent *et al.*[4353] as the least stressing. Vitamins and minerals in appropriate amounts must be supplemented. The water necessary will, of course, depend mainly on activity and the environmental temperature. If we assume a daily water output of 2500 ml (about $^1/_4$ of the heat lost by evaporation), then the water input must balance this amount: 2200 ml in the food and water and 300 ml from metabolic water.

Section 3. Maintenance of Man in Space

The first consideration for the development of a space environment is that of a container. The shape is of no consequence, except during exit from and re-entry into the atmosphere of the earth. This container should, of course, be capable of withstanding a pressure differential equivalent to the selected internal pressure and ideally should be completely sealed. The latter is probably not possible in that any space vehicle containing man will necessarily have a hatch— the absolute sealing of which is, except for extreme measures (such as welding), impossible; and even if this is accomplished, one must contend with the problem of the permeability of metal containers to various gases.

The next step, then, is one of modifying this container so that it supports life, preferably by the use of light weight systems. We may consider three basic systems:

(1) The simplest system to construct is one in which everything that is needed by the occupant is carried along on board, *i.e.* oxygen, food, water, etc., and the wastes such as carbon dioxide, water, feces are either absorbed by chemical absorbers or dumped overboard. Such a system is useful for flights of only a few days to a week, because the weight of such a vehicle increases linearly with the length of time one desires to spend in space.

(2) The slope of the weight-time curve may be decreased by the recovery of water from wastes, the reduction of carbon dioxide to carbon and oxygen, growth of food from wastes, reactivation of chemical absorbers, etc. However, these methods requiring an internal energy source only lengthen the time one may exist in space—perhaps to a few weeks if system weight is a limiting parameter.

(3) The ultimate goal in the maintenance of life in space is to achieve a system that will support life for an indefinite period. In such a system the required energy must come from some source external to the vehicle, such as the sun. This closed system may be of essentially one of two basic types: (*i*) A so-called "natural" system in which an attempt is made to duplicate the environment of earth. Photosynthetic organisms utilize man's waste products and energy from the sun to produce oxygen, and the increase in plant material harvested for food. (*ii*) An artificial system in which waste products are broken down by physical methods to produce oxygen and water. Waste products may also be converted into food by the proper use of catalysts.

1. Natural (Photosynthetic) Systems

In attempting to package the "environment" of earth into a small space, one is confronted with a number of problems. What plant is the most efficient in absorbing carbon dioxide and in the production of oxygen? What plant or plants has an AQ (assimilatory quotient = CO_2 taken up/O_2evolved) compatible with the RQ of man? Can these plants be eaten, and, if so, do they contain adequate concentration of fat, protein and carbohydrate? Are any toxic products produced by photosynthetic or respiratory processes of the plants? How much light do the plants need, and what wavelengths are most suitable? What temperature is optimum for the growth of these plants and is this temperature compatible with the temperature requirements of man? Will these plants utilize the waste products of man for growth? After these problems have been satisfactorily solved, one may then proceed to design the apparatus for a complete system.

In answer to the first question raised above, it is probable that algae are the organisms of choice. As a group they may be characterized as having the highest photosynthetic rates in the plant kingdom. Furthermore, they may be grown in liquid cultures in illuminated tanks through which cabin air may be pumped. Much of the early work of Myers[1360, 1361] was with *Chlorella pyrenoidosa,* a green alga. Such an alga will have an AQ of 0.7 if grown on nitrate or 0.82 if grown on ammonia or urea. At a wavelength of 6800 AU a suspension containing 10 g/l will absorb 97% of the incident light at a thickness of 0.4 cm. Thus, in order to provide a gas exchanger suitable for the maintenance of man, Myers estimates that 2.3 kg of *Chlorella* would be necessary in a total volume of 80 ft^3. He also estimates that the power required per man would amount to approximately 10 h.p. Unfortunately, the overall efficiency of such a system is less than 2%. Thus additional heat will have to be dissipated. However, by selecting wavelengths in the visible region and by maintaining optimal environmental conditions, this efficiency may be increased to about 18%. The exchanger will produce 23 g dry weight of algae/h of which the protein content is approximately 50%. As mentioned in the second section, this does not coincide with what may be termed an ideal diet. Human urine may provide a large fraction of the fixed nitrogen (1.8g/h) and mineral salts (1.2 g/h) necessary for the growth of the algae.

In later experiments Myers[1362] found that the blue-green alga *Anacystis nidulans* grown at 39° C would approximately double the production rate of *C. pyrenoidosa* which is grown at 25° C. However, he discovered[1363] that *A. nidulans* required a relatively high pH the growth, and consequently, if the CO_2 concentration were allowed to get too high, the algal solution pH would drop and photosynthesis would be inhibited. Consequently a screening program was initiated to select the most desirable algae for use as a gas exchanger. Krall and Kok[1355a] give the following algae selection criteria: (*i*) High growth rate; (*ii*) Suitable AQ; (*iii*) Compatible nutritional and pH requirements; (*iv*) Illumination response; (*v*) Desirable engineering characteristics; (*vi*) Tolerance for system poisons; (*vii*) Minimum algal noxious byproducts.

Other investigators are less conservative in their estimates of the quantities and volume of algae required. Bassham[1338] estimates that 1 kg of algae is sufficient to maintain one man for one day, and, furthermore, a much smaller volume than 80 ft.^{3} is necessary. Burk[4347] claims that 0.25 kg of a thermophilic algae (TX 71105) is sufficient to maintain one man for one day. These algae may be grown in concentrated (10%) solutions with very high light intensities. Thus, reducing the volume requirements to approximately 3 ft.^{3}/man/day.

At this point it is obvious that we are a long way from describing a closed system which will sustain man for an indefinite period of time. A few of the major obstacles are as follows: (*i*) Power requirements—can we get sufficient energy from the sun? (*ii*) Overall system efficiency; (*iii*) Nutritional value and palatability of algae (*Chlorella* have such a high composition of protein (50%) and low composition of carbohydrate (30%) that carbohydrates may have to be added to the diet); (*iv*) Toxic by-products of algae metabolism (Gafford[1350] reports a linear increase in the concentration of carbon monoxide produced by a culture of *Anacystis nidulans* in a closed system); (*v*) May the waste products of man be utilized directly by algae, or must they first be processed?

2. *Artificial (Physical) Systems*

As mentioned earlier the simplest type of system is one in which food, water, and oxygen (under high pressure or in liquid form) are carried on board the space vehicle along with chemical absorbers for carbon dioxide, water, and other wastes. A number of these absorbers have been considered by Bowman[4343]. Furthermore, this type of system has been used successfully in balloon flights[4366, 1369].

Systems of the above type are of value only for limited periods if one considers system weight as a limiting parameter. Thus, we must replace the photosynthetic system with some "non-living" system in order to progress to our ultimate goal of a completely closed system that will sustain man for an indefinite period of time. Bowman[4342] has proposed a number of ways in which this may be accomplished:

(1) Decomposition of CO_2 to oxygen and carbon requires that a carbon-oxygen bond be broken and this requires a considerable amount of energy, which may be high temperature or an electrical discharge. However, the reaction is not complete to carbon and oxygen, since carbon monoxide is formed in the process along with the oxygen. The carbon monoxide may be reacted with itself in the presence of a platinum catalyst at 250° C to produce carbon and carbon dioxide—and the carbon dioxide formed is then recycled. One may also react carbon dioxide with hydrogen (formed from the electrolysis of water) to form carbon monoxide and water. The carbon monoxide formed may then be decomposed in a number of ways.

(2) Carbon dioxide may be reacted with some metal to give carbon and the metal oxide. The metal oxide is in turn electrolyzed to oxygen and the metal. Lithium, which forms many low melting point eutectics, may be suitable for such a process.

(3) Carbon dioxide may be reacted with calcium oxide or calcium hydroxide to give calcium carbonate. The calcium carbonate is in turn reacted with hydrogen at red heat to give carbon, calcium oxide and water. The water may then be electrolyzed to give oxygen and hydrogen.

(4)

$$
\begin{array}{lcl}
4CaH_2 + 2CO_2 & \longrightarrow & C + CH_4 + 2H_2 + 4CaO \\
CaO + H_2 & \longrightarrow & CaH_2 + H_2O \\
CH_4 + 2O_2 & \longrightarrow & CO_2 + 2H_2O \\
2H_2O & \longrightarrow & H_2 + O_2
\end{array}
$$

These reactions are fairly involved; however, they may result in fewer side products.

(5)

$$
\begin{array}{lcl}
2C_2H_2 + CO_2 & \longrightarrow & 2H_2O + 5C \text{ (German patent 112,410)} \\
CH_4 + CO & \longrightarrow & H_2O + C_2H_2 \text{ (hot tube)} \\
CO_2 + H_2 & \longrightarrow & CO + H_2O \\
CO + H_2 & \longrightarrow & CH_4 + H_2O \text{ (cobalt, at 300° C)}
\end{array}
$$

(6)

$$
\begin{array}{lcl}
CH_4 + N_2 & \longrightarrow & 2HCN + 3H_2 \\
CO_2 + 4H_2 & \longrightarrow & CH_4 + 2H_2O \\
2HCN + CO & \longrightarrow & H_2O + N_2 + 3C \\
CO_2 + H_2 & \longrightarrow & CO + H_2O
\end{array}
$$

This series is of dubious value in that one of the products, hydrocyanic acid, is extremely toxic.

(7) Another tempting solution to the oxygen recovery problem is the direct utilization of carbon dioxide to form foodstuffs. As an example, in the synthol process, carbon monoxide (obtainable from one of the above reactions) is reacted with hydrogen gas at elevated temperatures and pressures over an iron catalyst to produce a mixture of olefins and water, plus some undesirable compounds which would have to be recycled.

Bowman[1342] has also listed a number of ways in which foodstuffs may be artificially produced from human waste materials. (*i*) *Fats.* The olefins produced in (7) may be oxidized by oxygen or ozone to give fatty acids. In the German *oxo process* the olefin is passed over a cobalt catalyst with carbon monoxide and hydrogen at elevated temperature and pressure. This results in the formation of an aldehyde of the structure RCH_2CHO containing one more carbon atom than the original olefin. This aldehyde may then be converted to its corresponding acid by oxidation. One of the by-products produced in the synthesis of fatty acids is propylene, which may be reacted with chlorine (obtained from the electrolysis of sodium chloride, which may be obtained from sweat or urine) to form a chloro compound. This compound yields glycerol when treated with sodium hydroxide (also formed by the electrolysis of sodium chloride). The glycerol may then be reacted with the fatty acids to produce fats. (*ii*) *Proteins*. Protein synthesis presents the biggest problem. Amino acids may be synthesized and given as food or combined into short chain polypeptides. However, the synthesis of complex proteins is another matter. Perhaps the use of nucleic acids as catalysts may be the answer. (*iii*) *Carbohydrates*. Here again we are faced with a complex problem. Monosaccharides may be formed by the polymerization of formaldehyde, but this leaves much to be desired, if only from the standpoint of palatability.

Thus far we have considered two basic systems for the control of the gaseous environment as well as the problem of nutrition. However, there are a few problems that may be solved only by physical methods. The first of these is temperature control. In a space vehicle there are essentially only two ways in which heat may be exchanged with the space environment. The first of these is to discharge mass from the ship after it has "soaked up" an amount of energy (heat) from sources within the ship such as the man and electrical equipment. An example of this would be a simple water evaporative system. In this system, water is evaporated within a heat exchanger at low pressure; with the vapour formed vented to space. The second method of exchanging heat is by radiation exchange between the vehicle and its space environment. The net exchange may be controlled to some degree by having a venetian blind arrangement on the surface of the ship. One side of the blinds has a high solar absorptivity and a low emissivity. The other side has the opposite. Thus, the heat loss or gain of the vehicle may be controlled at will. Hence, internal temperatures may be controlled within desired levels. This second method is obviously the one of choice for space flights of very long duration.

Another problem that must be handled by physical methods is that of ionizing radiation. It is probable that attempts to shield primary cosmic radiation will be ineffectual in that the energy levels are so high. Thus, one can only hope to slow the particles down, and in this process secondary radiations are given off which in turn would have to be shielded. Fortunately, however, the intensity of cosmic radiation beyond the Van Allen Radiation belts is probably fairly low. Tobias[1374] estimates that the cosmic ray level outside the earth's magnetic field is approximately 25 mrad/day. Of much greater concern to space vehicle occupants are the Van Allen radiation belts and the possibilities of solar flares. Prophylactic treatment against radiation involves the use of compounds that are at the present time too toxic[1347b], Therapeutic measures such as the use of bone marrow should prove useful, but the best method of radiation protection involves the use of shielding. Singer[4370] gives four possible ways in which protection may be afforded from Van Allen radiation:

(1) *Shielding*. An outer layer of lead reduces the radiative processes of protons by introducing a high Coulomb barrier. This outer skin may be placed away from the inner structural skin to act as a meteor bumper. The skin of the vehicle is made of low Z (atomic number) material to reduce the radiation from lead; low Z materials also have a higher stopping power per gram per cm² than lead. The inner layer of hydrogenous material serves to fragment heavy primaries of the cosmic radiation and thus reduce their biological effectiveness.

(2) *Shadow shielding*. The theory of trapped particles shows that they spiral mainly at rights angles to the line of force (earth's magnetic field). Therefore, a shielding ring (rather than a shell) may be sufficient, giving a weight saving of perhaps a factor of ten.

(3) *Magnetic screening*. This method also makes use of the fact that the incident radiation is very strongly peaked in the direction perpendicular to the line of force. By putting a coil around the space station with its axis parallel to the line of force, we can create a small-scale dipole field which turns away the incident radiation.

(4) "*Space sweeper*". If a large un-manned vehicle is sent out in front of the manned vehicle a channel will be "swept-out" through which the manned vehicle may pass, the un-manned vehicle having absorbed a large portion of the radiation.

Perhaps the most expedient solution to the Van Allen Radiation problem is to stay away from it, *i.e.*, exit the earth from a polar launch and then remain sufficiently far away from the earth that the radiation level is relatively low, or to pass through these radiation belts at high velocity to keep the total dose received as low as possible.

Still another problem to be considered is that of decompression of the space vehicle. This, as is the occurrence of a solar flare, is one of the primary accidental hazards facing an occupant of a space vehicle. Such an event could be caused by structural failure of the space vehicle, or by puncture of the vehicle by a meteoroid. If the decompression is rapid, the pressure differential created across the thorax may cause rupture of the lungs. Luft and Bancroft[1357] consider 80 mm Hg to be the maximum pressure differential that can be safely withstood. If the pressure drop is slow, a high pressure differential is not developed and the problem then becomes one of dysbarism and/or hypoxia. Konecci[1355] has demonstrated that a 0.005 in.² hole in a cabin with a pressure of 14.7 psia (pounds/in^2. abs.) will leak at about 10.8 lb./h, or a 120 day oxygen supply for one man would be lost in just one day. Protection against such an event may be accomplished by construction of a double walled vehicle. The question then arises: Where should such a second wall be placed? One answer is to place the wall external to the structural wall of the vehicle to act as a meteoroid bumper[4381]. Another method would be to place the wall internal to the main structural wall or to place a "wall" in close proximity to the space cabin occupant, a space suit. Vail [4375] has listed a number of requirements for such a suit, the ventilation of which is discussed by Webb and Klemm[4380].

Should long term weightlessness prove deleterious to man, it will be necessary to create an artificial gravity within the space vehicle by rotating the vehicle about its axis. The radius of such a vehicle should be rather long in order to keep Coriolis forces on the occupants to a minimum[4347a, 4351a, 4356].

Section 4. Adaptation to a Space Vehicle Environment

Thus far we have dealt with methods for the protection of man in a space vehicle. Attempts have been made to provide an environment similar to his natural earth environment. But, how can we be sure that our artificial environment really is optimal? The answer of course, is that we can't. We cannot answer this question until man actually flies about in space. It has been speculated that the psychological stress of long term confinement may be the weak link in the chain to prolonged space flight. Such a situation cannot be simulated on the ground, because a subject always knows that he can voluntarily curtail the experiment. However, we do have subjective information from balloon occupants[4366, 4369], and some information from ground isolation studies[4367] concerning sensory deprivation and monotony.

At this point, the question may be raised: What is there about space flight that cannot be controlled? Radiation, both ionizing and non-ionizing may be shielded or avoided. The temperature and pressure will be controlled. An artificial gravity (even magnetic fields) may be introduced. Compounds usually seen only in trace amounts such as ammonia from urine or methane from flatus (*i.e.* gas or air in stomach or intestine) may build up to toxic levels in a closed space vehicle; but toxic compounds may be removed by adsorption or broken down by physical methods. Aside from isolation, only one possibility is left. Time itself.

If a space vehicle is accelerated to relativistic speeds (approaching the speed of light) we must contend with an increase in the relativistic mass of the space vehicle, and hence, everything within it. This extreme velocity will also cause a change in the frequency of some oscillator within the space vehicle, such as a "metabolic clock" within a man. A consideration of some of these relativistic principles is given by Pierce[4365]. Such considerations are at the present only of academic interest. Present day satellites travel slower than the speed of light by a factor of about 3.10^4.

Of more immediate interest is the problem of biological rhythms (see pp. 369–371) which may be modified in a space vehicle where the earth, moon, sun relationships normally experienced by a man or animal on earth have been altered. For a thorough discussion of biological rhythms, the reader is referred to Vol. 25 of the Cold Spring Harbor Symposia on Quantitative Biology entitled *Biological Clocks* (see also references[1144, 1201]). The usual stimulus to rhythm alteration is light. However, it is a possibility that other factors have stimulus value. Brown *et al.*[4346b] has shown correlations of metabolic activity and magnetic fields. How will man react when he is removed from normal gravitational and magnetic forces? This as well as other questions await the flight of man into outer space to be answered.

PART VII

Graduate Training in Human Biometeorology

by

FREDERICK SARGENT

Section 1. Why Provide Graduate Training in Biometeorology?

There are both academic and practical reasons for training graduate students in biometeorology. These reasons are over and above the simple one that students are interested in learning about this intriguing subject. In recent years the traditional boundaries between the various sciences have been steadily crumbling. Interdisciplinary fields have grown rapidly in number Biometeorology is actually just one of those scientific activities; it utilizes the methods and concepts of both biology and meteorology to study Nature. These interdisciplinary fields are complex and should ultimately force universities to broaden the bases of their graduate programs. Since this broadening has not yet taken place, we must do three things for the young scientist. We must give him a sound training in a major area and a firm working knowledge of an interdisciplinary field (in American universities such training constitutes the "minor"). In addition, he must learn to work in a team. Because few scientists are sufficiently broadly trained to solve many of the complex problems of the interdisciplinary fields, team research has provided the stop-gap solution. Investigators with diverse and specialized training pool their talents in the study of these problems. The scientists of the present generation must have some idea about how to work efficiently and productively in such a group effort.

Early introduction to the conduct of team research can be made by taking advantage of the diverse orientations of the students who enroll in courses in biometeorology. In the author's classes, for example, there have been physiologists, geographers, animal scientists, zoologists, physical educators, veterinarians, and psychologists. Therefore, one generally has ample opportunity to raise the problems of the interdisciplinary approach and to begin training the students in team research by having small groups undertake special projects.

An even more important academic matter concerns training students to generalize from complex inter-related facts. The average student can learn facts. His chief difficulty is failure to see the relatedness of facts and inability to arrive at general concepts based on these relationships. Biometeorology is one frame-work within which such training can be undertaken. An even more fruitful area is ecology, for there one must think holistically in order to comprehend the concepts. Advances in the sciences are made not by data-collectors but by generalists, investigators who have the capability of seeing new relationships among facts.

On the practical side there is a definite and growing need for individuals trained in biometeorology. Military, governmental, and academic institutions need these people for teaching and, primarily, for conducting research in environmental physiology, environmental protection, and medical geography. When the fact that such training is being given becomes more generally known, it is probable that other organizations, such as the life insurance companies and the aviation and air-conditioning industries, will realize that they too can profitably employ a biometeorologically trained biologist or geographer. The new field of "space biology" is another area where the biometeorologist has become a useful member of the teams endeavoring to provide a suitable "closed ecological system" which will sustain man during a journey into the realms beyond the earth's atmosphere.

Section 2. The Prerequisites for Training in Biometeorology

The major divisions of human biology which must be dealt with in biometeorology are physiology and psychology, pathophysiology and abnormal psychology, and some aspects of medicine and public health. Consequently, students enrolling in courses in biometeorology must have some background in physiology and psychology, and each should be conversant with the basic elements of meteorology and climatology. The ideal schedule of prerequisites includes physics, chemistry, biology, mathematics, statistics, meteorology, climatology, mammalian or medical physiology and pathophysiology, and psychology; sociology and anthropology are desirable. Other prerequisites are, apart from English, history, economics etc., a good reading ability in at least two modern foreign languages. The language requirement is an essential one for much of the current and past biometeorological literature (whether books or journals) is published in German.

Courses in biometeorology should constitute a minor in the student's graduate program. The students who elect this field as a minor should be working for a doctorate in a major field such as physiology, geography, hygiene, zoology, or psychology. A doctorate in biometeorology would be ridiculous within the conceptual frame of modern professional teaching.

Section 3. The Academic Environment

In what academic environment can biometeorology best be taught? In 1897 Ward[4400] made a vigorous plea for meteorological and climatological instruction in the medical school. A survey conducted at the time indicated that while deans were generally in favor of such courses, few medical schools actually taught them. The chief reasons Ward offered for such training were the need for medical climatological research and the need for intelligent practice of climatotherapy. Similar opinons were voiced by Solly[4399] in 1904 and Loomis[4390] in 1906. These suggestions, however, produced little or no biometeorological instruction, and it was not until fifty years had passed that formal training of any kind did begin. The present graduate programs are, in so far as the author has been able to learn, limited almost entirely to the United States. In Europe there are lectures and graduate seminars, but apparently no comprehensive curricula.

The courses in America are offered under a wide variety of circumstances. For a number of years Lee[4389] taught courses jointly with the Departments of Geography and Hygiene at Johns Hopkins University. At the University of Illinois biometeorological training has been a joint effort among the Departments of Geography and Physiology and the Physical Environment Laboratory[4394, 4396]. At the University of Washington the training has been jointly done between the Department of Meteorology and Climatology and the Department of Physiology and Biophysics (K. J. Buettner, pers. comm.). At the State University of Iowa there has been a seminar in environmental physiology conducted within the Department of Physiology of the School of Medicine (G. E. Folk, Jr., pers. comm.). At the University of Pittsburgh environmental physiology has been a course in the School of Public Health (H. S. Belding, pers. comm.). At the State University of Pennsylvania H. Neuberger (pers. comm.) has for some years given a seminar in biometeorology. This seminar was started by H. Landsberg in 1942. At the University of Missouri W. E. Johnson has taught environmental physiology within the Department of Animal Husbandry.

Only two general points emerge from this catalogue. Biometeorological training is only offfered to graduate students. The courses generally occur only in those major universities that are well equipped with the physical facilities necessary for biometeorological investigation. Such universities assuredly provide the ideal academic environment. The author would, however, reiterate the early remarks of Ward, Solly and Loomis: the concepts and fundamentals of human biometeorology must be introduced into the training of physicians. The best frame-work within which to make this innovation is the rapidly developing area of human ecology, which, in recent years, has become a major concern to many medical educators.

Section 4. Didactic Training

The formal training can be divided among four courses: one on the fundamentals of biometeorology, one on techniques of experimental biometeorology one on medical geography, and a seminar. Let us consider these four courses in turn.

1. *Fundamentals of Biometeorology*

A difficult problem immediately presents itself: What are the fundamentals? In the author's opinion there are relatively few firmly established concepts which belong only to biometeorology. There is a real need for these fundamentals to be separated from the mass of conjecture and speculation that dominates so much space in the journals and monographs. Since the students must be made to realize this state of affairs—and it is really a stimulus to most of them to find this fact out—the best approach is to expose the students not only to established facts and concepts but also to choice examples of delightful nonsense and fancy speculation. At all times the assumptions made in order to arrive at conclusions must be clearly distinguished, discussed, and evaluated. If these students are to be trained to make significant contributions to the advancement of biometeorology, they must be given practice in making independent and critcial judgments about the quality of biometeorological publications.

Most graduate students who elect to take courses in biometeorology know very little about meteorology and climatology. It is, therefore, usually necessary to begin with a general discussion of the meteorological elements and their inter-relations which constitute the weather, of air masses and fronts, and of "weather types". Next the area of climatology must be considered and here special emphasis should be laid on the several ways by which climates may be classified.

At this point it is advantageous to introduce the student to the literature dealing with the relationships among sun, weather, and man. Because there is some evidence[4383] that solar events may be correlated with human health and behavior, the idea must be presented that when thinking about the physical environment within which man resides, we must not limit it to the troposphere but perhaps we must extend that environment at least to the sun.

The next general matter to be dealt with is the use of statistics in biometeorology. Statistical procedures in wide use range from folk-lore through what has been aptly termed "eye-ball analysis" to a variety of formal devices such as correlation coefficients, analysis of variance, Chi-Square test, and the n-method. Statistics in biometeorology are most commonly used to demonstrate a significant association between weather and some aspect of human physiology or pathophysiology. Here the basic assumption frequently made is that if sufficient numbers are employed in the analysis, the atmospheric environment represents the only important variable; other possible environmental or non-environmental influences tend to be neglected. Although the author is not aware of any proof or disproof of the validity of this assumption, the fact remains that such an assumption does lie behind the use of statistics in biometeorology.

Many drugs and biological preparations must be standardized in terms of their physiological or pathological effects on a particular laboratory animal. In order for the standardization to be uniform, it has been found that the inherent biological variability of the animal must be reduced as much as possible. Such factors as sex, body size, litter, genetic background, and nutrition must all be closely regulated. In addition, to achieve the most reliable results, the standardization must be performed in a facility the physical environment of which is maintained constant and uniform—at least with regard to light, temperature, moisture, and air motion. This important application of biometeorology can be illustrated with a variety of examples from the fields of pharmacology, bacteriology, serology, nutrition, and experimental pathology.

The first basic concepts which must be considered in some detail are those of biological variability and homeostasis. Both are important generalizations in human biology and, in the author's opinion, homeostasis is actually only a special case of the broader concept of biological variability. The latter deals with the degree of similarity and dissimilarity among human beings from the point of view of their constitutional characteristics, which can be classified according to morphological features, chemical and physical properties and constituents of the internal environment, physiological processes, quantity of reserves, and behavior. Many of these characteristics are genotypic; some are phenotypic. According to the concept of homeostasis, the function of many physiological processes is to regulate the chemical and physical properties of the internal environment so that their variability is minimized: a relative constancy of the internal environment is a necessary condition for the most efficient operation of cellular processes and the body as a whole. The limits within which these constitutional characteristics vary are called the "normal limits" and these limits are generally arbitrarily defined as plus or minus two standard deviations on the basis of single measurements made simultaneously on a large population tested under standardized conditions. When a single individual or a small group are studied repeatedly with respect to these characteristics over a period of months or years, the order of magnitude of the variability is the same as that defined by measurements on the large group [4397]. Now one assumption of biometeorology is that when this variability is significantly correlated with the weather or the seasons, the variations might be caused by the changing atmospheric environment. This assumption has neither been validated or critically examined from the viewpoint of biometeorology. Since, whether we consider variability within one individual or variability between individuals, we deal with limits of equivalent magnitude, it may well be that the assumption is fallacious. In the author's opinion this problem is one most urgently in need of thorough investigation. Certainly the student should be appraised of this assumption and its implications.

The next concept which must be considered is that of homeothermy. This is a special instance of homeostasis and involves detailed consideration of the physical and physiological processes that regulate body temperature [4386]. This concept is one that can be treated quantitatively; it is an excellent example of what Buettner[4384, 4385] has called quantitative biometeorology.

A further basic concept is that of acclimatization. When exposed to unusual cold, heat, or high altitudes of mountains, the human body can make remarkable physiological adjustments which gradually overcome the initial deleterious effects of those new atmospheric environments. A corollary of this concept is that of dysacclimatization. Both early in acclimatization and after weeks of exposure, clinical deterioration may develop. These failures of acclimatization are the climatic diseases and most of them can be reproduced in the laboratory under controlled conditions. Although in the laboratory acclimatization can be achieved in two or three weeks, there is evidence from the field that further acclimatization may occur after years or even generations of exposure. An important point to bear in mind, however, is that there are limits of heat, cold, and altitude beyond which the body cannot acclimatize; indeed beyond which one can only tolerate a brief exposure.

Although the concept of acclimatization has a firm experimental basis, there is little unanimity regarding the mechanisms responsible for the process. What are the relative importance of cardiovascular, metabolic, and endocrinologic adjustments? Do the processes of acclimatization to heat, cold, and altitude have anything more in common than improved tolerance for unusual environments? For example, are they each special cases of the general adaptation syndrome of Selye [4398]? In rats at least they are probably not related to this syndrome [4388]. Can man cross-acclimatize to heat and cold simultaneously or does one process interfere with the other? These and other major problems should serve to demonstrate to the student that we cannot define acclimatization precisely; we can only describe it in terms of the observations made in the field or the laboratory.

The idea of meteorotropism [1387] is the final concept which should be dealt with. The basic observation underlying the meteorotropism is that cases of a particular disease or episodes of particular behavior tend to occur in groups closely linked in time or space. The assumption made, especially when the sample is large, is that the grouping is a manifestation of the effect of the atmospheric environment. By appropriate statistical procedures tests are made to prove that the grouping is neither merely random nor cyclic. If neither, the biometeorologist searches among the atmospheric elements and weather types for a correlate of the biological events. A significant correlation establishes a meteorotropism. Spatial meteorotropisms are in the province of medical geography. Temporal meteorotropisms may be related to seasonal or daily variations in the atmospheric environment or to events on the surface of the sun. The assumption that statistical correlation with some meteorological element, weather type, or measure of solar activity establishes causality had not, however, been substantiated under controlled conditions in the climatic chamber. For didactic purposes meteorotropisms can be treated systematically, *i.e.* according to cardiovascular system, nervous system, endocrine system, and so on. Laboratory evidence can be adduced to examine the pathophysiological mechanisms which have been suggested to explain meteorotropisms. These considerations serve as an excellent introduction to the problems of the natural history of disease. Because of the absence of adequate experimental observation, much of this material is speculative. The point which must be emphasized is that the patient must be taken into the climatic chamber along with healthy controls. On both quantitative physiological and biochemical measurements must be made by fully validated and precisely discriminatory methods. Only by these means can one hope to explain fully the mechanism of the meteorotropism.

2. *Techniques of Experimental Biometeorology*

A second course which is very important in the training of graduate students is one which acquaints them with the methods of experimental biometeorology and which also provides them with an opportunity to observe for themselves some of the fundamentals of this field. In brief such a course should include the following: (*i*) Methods for assessing the atmospheric environment; (*ii*) Special methods and devices for measuring the physical environment of climatic chambers; (*iii*) Procedures for assessing the response of man to the atmospheric environment, particularly those of thermometry and partitional calorimetry for they are not dealt with in the usual courses in physiology; (*iv*) Experiments demonstrating the principles and concepts of environmental physiology and illustrating the use of the various physical and physiological measuring devices.

3. Medical Geography

There are few courses which deal with medical geography. At the University of Illinois one is being planned and it will supplement a curriculum in human ecology which is also in the planning stages. A broad introductory course is urgently needed both for reasons listed earlier and to round out graduate training in biometeorology. The course which we have in mind would acquaint geographically trained students with the concepts of medical geography so that they could work with teams which included medically trained individuals. The prerequisites for this course would be geography, human ecology, and the fundamentals of biometeorology.

The general field and the important concepts of medical geography have been described by May [4391-4393] (see pp. 598–604). Our course would build on this background and would include the following considerations: (*i*) The historical development of medical geography; (*ii*) The definitions and descriptions of communicable, metabolic, and behavioral disease; (*iii*) The statistics of disease, their collection, tabulation, standardization, and validation; (*iv*) Cartographic presentation of patterns of disease; (*v*) The environmental and biological factors responsible for disease, *e.g.* insect and animal vectors, variations in host and infective agent, ethnic factors, socio-economic and public health factors, soil, topography, weather and climate, agriculture, and radioactivity, and their cartographic representation; (*vi*) Interpretation of similar patterns of disease and biological and environmental elements which may indicate causal relationships, and (*vii*) Problems of medical geography demanding critical thought and investigation such as determinism, spatial meteorotropisms, and the translation of medical geographical findings into questions which can be examined in the laboratory or under controlled field conditions. Such a course as this one might be useful not only to the geographer but to the medically trained individual who has had some experience with environmental medicine.

4. The Seminar

For students who have had some exposure to fundamentals, concepts, and generalizations, informal discussion of biometeorological problems is both stimulating and invaluable training. When students are assigned topics and articles to discuss before their fellows, a lively exchange usually evolves, especially when they present not only sound material but also poorly controlled observations or speculations that are not justified by the experimental data. By these means the student acquires an ability to think and talk on his feet, finds that much of what he thought was firmly established is actually not so secure, and, most importantly, learns critical judgment.

Section 5. Field Experience

Biometeorology, and especially medical geography, are not sciences which depend for their advancement solely on laboratory investigation or research in statistical archives or libraries. Much research must be conducted in the field. Therefore, a vital element in graduate training must be actual field work on a carefully conceived problem. This phase of his work should constitute the original research the student does for his doctorate. In order that useful work be accomplished, it is necessary that the student become part of a team sent out from an institution which frequently does field research in industries, in communities, or among isolated populations. In this way he can be indoctrinated and supervised by competent field workers. Since most of his career in medical geography, for example, will be spent in doing such field investigation, it is well that early in his training he learns to work with a team, to be responsible for a share of the over-all study, and about the planning which must precede successful field work. Not only is the actual field study valuable training, but the analysis of the observations made and their interpretation and reporting in thesis and technical publications are vital as ways of integrating all his previous didactic work.

Section 6. Research in Climatic Chambers

For some students the problems they desire to investigate lend themselves to study under the controlled conditions of the climatic chamber. These students must have had training in the techniques of experimental biometeorology prior to undertaking independent research. For these students the experience of working with a competent environmental physiologist is just as valuable as that of field work for the men whose problems demand that type of approach or whose career demands this training.

Section 7. Traineeships in Biometeorology

Since there is a definite need for young people trained in biometeorology and since training is expensive both for the graduate student and in terms of the physical facilities required in the training, the author [1395] proposed two years ago that national governmental agencies should establish traineeships in biometeorology for competent graduate students. The primary aims of these traineeships would be to provide financial support for the student so that he could, first, undertake the necessary didactic work and then conduct a piece of independent research either in an establishment having a climatic chamber or in the field. The most advantageous way to utilize the physical facilities, the instructors available, and the training programs already in existence would be to support those programs with training grants. By this device qualified graduate students might be encouraged into a field where they are urgently needed. Growth and development in biometeorology depend on critical thinking and conduct of sound research. For research programs to be carried along, we must provide them with carefully trained young investigators.

Retrospect

by

S. W. TROMP

In the foregoing chapters we have tried to summarize the most important aspects of biometeorology, though there are obviously many aspects which could not be discussed. It is fully realized that, notwithstanding the overwhelming number of data accumulated during the past 50 years of research, biometeorologists still have a long way to go before they can solve all the important problems and fully explain the various observations made.

On reaching the beginning of Part IV, Chapter 1, the reader may have questioned the necessity for such an extensive review of the known physiological facts, which are usually published in various physiological textbooks and journals. After reading the next sections of the book, however, it may have become clear that this summary enabled the writer to present a considerably simplified and succinct explanation of the observed facts. Nonetheless, there were other reasons as well for recounting these physiological data, more especially for the benefit of the non-physiologically trained biometeorologist. Most books on biometeorology have hitherto presented an array of bare facts without any attempt to integrate them within a physiological context.

These physiological facts are scattered in various journals which are often not readily accessible to most biometeorologists, another reason for adopting our system.

As biometeorology is gradually developing into an independent border-science, it has been necessary to outline in a textbook those fields of physiology and meteorology which should be common knowledge of every student of biometeorology if he is to embark successfully upon new biometeorological research projects.

I hope that we have succeeded in providing the tools which will enable the future student to do the job. A vast field of study is still virgin soil and further scientific research may find new ways of utilizing biometeorological observations for the maintenance of health. At the present stage of medical science the physician is apt to forget that the human body and its physiological processes are closely integrated in the physical and chemical environment in which man happens to live. Although clinical treatment with drugs may bring temporary relief to the patient, it may not remove the actual primary cause of the disease. The observations to date suggest that a deeper understanding of biometeorological processes in general and of climatotherapy in particular might well remove at least some of the actual causes of a great number of diseases, thereby eliminating that recourse to innumerable drugs, which has become such a common practice in modern society. In its wider implications, moreover, biometeorology shows, more clearly than most other sciences, how closely the animate and inanimate worlds are integrated. It is this deeper understanding of the continuous interaction between the living and non-living worlds, which makes biometeorology one of the most fascinating and promising border-sciences of the twentieth century.

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CHAPTER 5. POSSIBLE INFLUENCE OF EXTRA-TERRESTRIAL FACTORS (PICCARDI EFFECT)

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PART III

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PART IV

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CHAPTER 2. BIOMETEOROLOGICAL EFFECT ON DISEASES (PATHOLOGICAL BIOMETEOROLOGY)

A. PRINCIPAL METEOROTROPIC DISEASES

Allergy

General

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PART V

Effect of Weather, Climate and Season on the Living World Surrounding Man

CHAPTER 2. EFFECT ON ANIMALS (ZOOLOGICAL BIOMETEOROLOGY)

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SUBJECT INDEX

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