BIOMETEOROLOGY

VOLUME 2

Part 1

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Proceedings of
The Third International Biometeorological Congress,
held at Pau, S. France, 1–7 September 1963
organized by
"The International Society of Biometeorology"

Edited by

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* Epidemiology and Biometeorology of Fungal Diseases of Plants. Mimeo. The Pennsylvania State University, Unpaginated, 1963.

** Reports published in the "International Journal of Biometeorology", Volume 8, Number 2, 1964.

INTRODUCTION

The Third International Biometeorological Congress, the official meeting of the International Society of Biometeorology (ISB), organized by the Secretariat of ISB was held from 1 to 7 September 1963 at Pau, Southern France.

The Congress program consisted of two plenary sessions and separate sessions of 15 working groups covering various special fields of biometeorology.

The plenary sessions dealt with the following subjects:

1. RECENT PROGRESS AND FUTURE LINES OF RESEARCH IN AGRICULTURAL (P. M. A. Bourke), PHYTOLOGICAL (R. D. Schein), ENTOMOLOGICAL (W. O. Haufe), VETERINARY (J. D. Findlay), and HUMAN BIOMETEOROLOGY (S. W. Tromp).
2. SIGNIFICANCE OF THE STUDY OF BIOLOGICAL RHYTHMS IN BIOMETEOROLOGY:
   Les rythmes biologiques des plantes et la biométéorologie (L. Baillaud);
   Periodicity Analysis. A Potential Tool for Biometeorologists (F. Halberg);
   Significance of Biological Rhythm Study for Human Biometeorology (A. Sollberger).

The Presidential address: A PROGRAM FOR BIOMETEOROLOGY (F. Sargent II), and the lectures given at the plenary sessions were printed in full length in the "International Journal of Biometeorology", Volume 7, Number 2, December 1963.

The papers presented at the Congress during the sessions of the specialized working groups, including summaries of the discussions, have been screened and edited by the Chairmen of the working groups and by the Chief-Editors (S. W. Tromp and W. H. Weihe) assisted by five Language Editors: W. A. Fairbairn and R. W. Gloyne (English); B. Primault (French), H. Brezowsky and W. Menger (German).

As only a restricted number of pages could be printed by Pergamon Press, several papers could not be published in full length and are given in abbreviated form in the original language only. Abstracts of the papers published in full length are given in English, German and French. The discussions following each paper are summarized in the summary reports of the chairmen of the working groups.

The papers of two of the 15 working groups have been published elsewhere. The papers of the working group on "Indoor Climate in Arid and Humid Zones" were published in a special issue of the International Journal of Biometeorology, Volume 8, Number 2, December 1964. This publication was supported by a grant from UNESCO. The papers of the working group on "Biometeorology and Epidemiology of Fungal Diseases of Plants", were published by the Pennsylvania State University (University Park, Pa., U.S.A.) with a special grant from NATO.

The Executive Board of the ISB wishes to avail itself of this opportunity to thank the Chairmen of the working groups, the Language Editors and Mr. R. E. Strange of Pergamon Press for their great help in the publication of these Congress Proceedings.

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PART 1

HUMAN BIOMETEOROLOGY

Chairman: D. Ordman

ASTHMA, WEATHER AND CLIMATE

ASTHMA AND TEMPERATURE CHANGE*

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Abstract — A study of emergency clinic visits for asthma at three major hospitals in New York City during September 1962, September 1961, and September–October 1957 revealed an increase in asthma visits during the onset of cold weather when heating was required. The most pronounced and significant increase occurred with the onset of the first or second such cold periods requiring heat. The pollen and mold counts in all three periods of the three years studied were low and the air pollution levels of sulphur dioxide, smoke shade and carbon monoxide were within usual values.

Zusammenfassung — Eine Untersuchung von Astmaanfällen an drei großen New-Yorker Krankenhäusern im September 1962 und 1961 sowie im September und Oktober 1957 zeigte eine Zunahme der Anfälle während des Einsetzens von kaltem Wetter, wenn geheizt werden musste. Das Anwachsen war am ausgeprägtesten und überzufällig beim Einsetzen der ersten oder zweiten solcher kalten Perioden. Die Pollen- und Pilzzahlen in allen drei Perioden der drei Jahre waren niedrig, der Spiegel der Luftverunreinigung mit Schwefeldioxyd, „Smoke“ und Kohlenmonoxyd lag im üblichen Bereich.

Résumé — L'étude des cas d'asthme de 3 grands hôpitaux New-Yorkais, étude faite en septembre 1962, septembre 1961 et en septembre–octobre 1957, a montré une nette augmentation du nombre des crises annoncées au cours des périodes de temps froid nécessitant le chauffage des habitations. La dite augmentation était plus sensible au début de la première et de la deuxième de ces périodes froides. Le nombre des grains de pollen et de spores de champignons était particulièrement faible durant les quatre mois étudiés. Le taux de pollution de l'air en dioxyde de souffre, en fumée et en monoxyde de carbone est resté parfaitement normal.

Asthma is a disease of wide prevalence causing much morbidity and some mortality. The onset and clinical intensification of asthma are ascribed to many factors some of which are emotional stress, bronchopulmonary infection, allergens, pollens, molds and spores, and environmental factors. Despite the wealth of material concerning asthma in the literature, there is little statistical documentation on the epidemiology of asthma.

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A study was made of the relationship between air pollution, meteorology, and asthma emergency clinic visits at three large New York hospitals for the years 1962, 1961, and 1957.

As a measure of outdoor temperature we employed the hours of heat required in residence apartments in New York City in accordance with the New York City Health Code. The latter requires that dwellings be provided with heat between the hours of 6 : 00 a.m. and 10 : 00 p.m. when the outdoor temperature falls below 55° F.

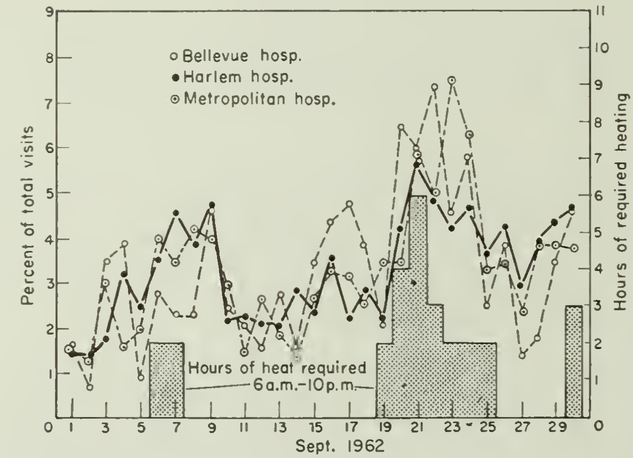

FIG. 1. Daily emergency clinic visits for asthma in percent of total visits for the period. Bellevue, Harlem, Metropolitan, Hospitals Sept. 1962

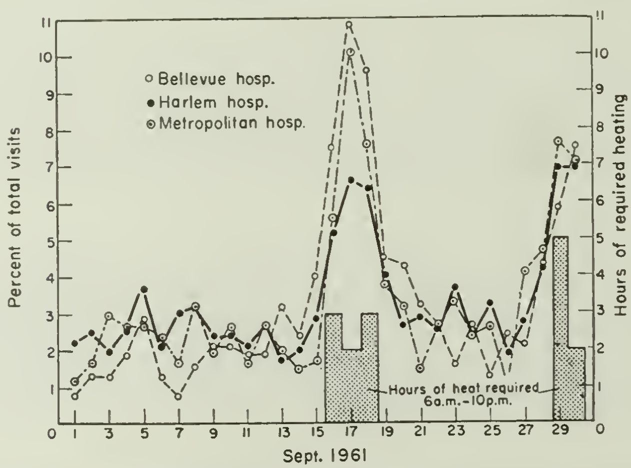

FIG. 2. Daily emergency clinic visits for asthma in percent of total visits for the period. Bellevue, Harlem, Metropolitan Hospitals Sept. 1961

Figures 1, 2, and 3 show the variations in asthma clinic visits by day expressed as a percentage of the total visits for the period under study, namely the month of September 1962 and 1961, and 16 September–15 October 1957.

The average daily number of emergency clinic visits for asthma for the critical period (the period of decreased outdoor temperature) as compared with

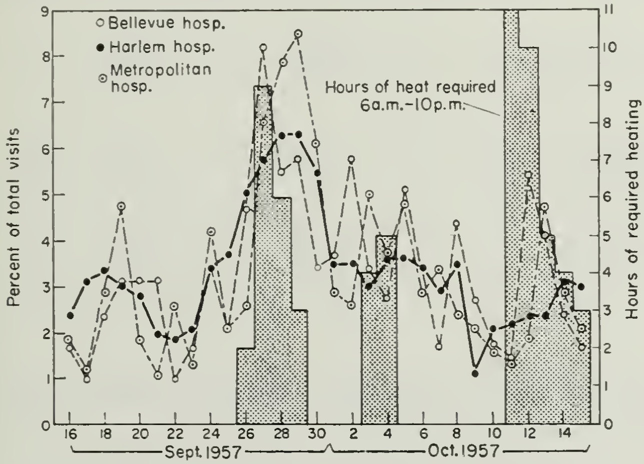

FIG. 3. Daily emergency clinic visits for asthma in percent of total visits for the period Bellevue, Harlem, Metropolitan Hospitals Sept. 16–Oct. 15, 1957

Table 1. Average Daily Number Of Emergency Clinic Visits For Asthma 1962, 1961, 1957

	Bellevue Hospital	Metropolitan Hospital	Harlem Hospital
1962			
1–18 September	12.0	23.2	39.7
19–26 September (Critical Period)	21.0	42.4	60.3
27–30 September	12.3	30.3	57.0
1961			
1–15 September	7.4	27.3	14.5
16–19 September (Critical Period)	30.5	60.8	44.8
20–30 September	12.9	40.2	24.1
1957			
16–25 September	6.6	9.0	25.0
26–30 September (Critical Period)	16.2	24.0	52.4
1–15 October	9.7	11.2	26.3

Table 2. Values of the Comparison of Asthma Visits of the Critical Period with Asthma Visits of the Prior and Subsequent Days

	Bellevue Hospital	Metropolitan Hospital	Harlem Hospital
1962			
Prior to critical period	<0.05	<0.01	<0.01
Subsequent to critical period	>0.05	>0.05	>0.05
1961			
Prior to critical period	<0.01	<0.01	<0.01
Subsequent to critical period	<0.01	<0.05	<0.05
1957			
Prior to critical period	<0.01	<0.01	<0.01
Subsequent to critical period	<0.05	<0.01	<0.01

the prior and subsequent periods is shown in Table 1. Table 2 shows the p values of the asthma clinic visits for the critical period (the period of decreased outdoor temperature) as compared to the prior period.

From these data it is clear that there exists a pronounced and statistically significant increase in asthma clinic visits with the onset of the first or second cold periods, that is periods requiring heating in accordance with the New York City Health Code. These significant increases in asthma visits are not related to pollens or molds in the atmosphere, and so far as we have been able to determine, the increases are not related to the levels of sulphur dioxide, smoke shade, carbon monoxide, or any other air pollutant now measured in New York City.

The findings disclosed by this study raise certain fundamental questions as to the cause for the sudden increases in asthma visits to emergency clinics. It may be that one or more air pollutants not now measured are responsible for this increase; such pollutants as those released at the onset of the heating season when equipment is newly fired, or such pollutants as dust or molds, lying dormant in or around radiators of enclosed spaces. Consideration must also be given to the extremely low levels of humidity brought about by indoor heating. Lastly, it is necessary to consider the effect of cold air as a physiological triggering mechanism in susceptible individuals.

It is our belief that the relationship between increased asthma visits and the onset of cold weather is a geographically widespread phenomenon.

KLIMATISCHE GESICHTSPUNKTE IN DER BEHANDLUNG DES ASTHMA BRONCHIALE

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Abstract — Climate, weather and seasons are of special importance in the case of asthma bronchiale. Attacks are more frequent in the warm humid air of southern Germany and in the cold dry air of the North Sea. The danger of asthma disposition is greater on wet than on dry ground. The increase of pollen in the air is not related to the incidence of asthma attacks. Climatotherapy is practised in moderately high mountains, in high mountains and at the North Sea. Too much protection may be favourable to recurrence. Stimulation by the climate must be dosed by selection of the place of residence, e.g. the microclimate.

Zusammenfassung — Klima, Wetter und Jahreszeit sind bei Asthma bronchiale von besonderer Bedeutung. Vermehrte Anfälle treten in Süddeutschland bei warm-feuchter, im Küstengebiet bei kalt-trockener Luft auf. Feuchte Böden erhöhen die Asthma-Bereitschaft erheblich. Vermehrung der Pollen in der Luft und Häufung der Asthmaanfälle zeigen keine zeitliche Korrelation. Klimatherapie wird im Mittelgebirge, im Hochgebirge und an der Nordsee durchgeführt. Zu starke Schonung kann Rückfälle begünstigen. Klimareize müssen durch Wahl des Expositionsortes, also des Kleinklimas, dosiert werden, wobei durch Verbesserung der Reaktionsfähigkeit die Wetterempfindlichkeit herabgesetzt wird.

Résumé — L'action climatique du temps et de la saison sont liés particulièrement dans le cas de l'asthme bronchitique. Les crises asthmatiques augmentent en Allemagne du Sud au cours de temps humide et chaud, sur la côte lors de temps froid et sec. La terre humide augmente la disposition d'asthme plus que la terre sèche. Il n'y a pas de relation simultanée entre la fréquence des crises asthmatiques et l'augmentation de quantité des pollens dans l'air. Le traitement climatique doit être appliqué dans les régions d'altitude moyenne, de haute montagne et au bord de la mer du Nord. Le climat sédatif trop fort peut favoriser les récidives. Le climat stimulant doit être dosé par le choix de la localité, c'est à dire par le choix du microclimat.

Meteorotrope Krankheiten und Saisonkrankheiten wurden noch 1952 voneinander getrennt betrachtet (de Rudder). Das Asthma bronchiale ist aber eine Krankheit, bei der Einflüsse von Klima, Wetter und Jahreszeit deutlich werden. Zum Verständnis der atmosphärischen Beeinflussung dieser Erkrankung muss das Ineinandergreifen aller Faktoren im Einzelfall analysiert werden. Nur dadurch kann man bei der klinisch bedeutsamen Krankheit zu therapeutischen Folgerungen gelangen.

Die Häufigkeit des Asthma bronchiale wird für verschiedene Gebiete etwas unterschiedlich angegeben, doch liegt sie etwa bei 1% der Bevölkerung. Nach v.

Knorre (1960) wurde für die Bundesrepublik (1952) 7.2‰ geschätzt. Quarles van Ufford (1958) gibt für 1949/50 für die Niederlande 9.3‰ an.

Bei der Analyse von 1000 Asthma-Anfällen fand Daubert (1959) für den Tübinger Raum (Süddeutschland) eine positive Korrelation mit subtropischen Meeresluftmassen, dementsprechend auch für Warmfronten und Okklusionen, dagegen weniger stark bei Kaltfronten. Bei Polarluftmassen waren Anfälle vermindert. Im gleichen Sinne beaobachtete Brezowsky (1960) für das Alpenvorland eine Steigerung von 36% für Wetterphase 4 (warmfeuchtes Luftmilieu) bei asthmoider Bronchitis und eine Steigerung von 11% bei gleicher Wetterphase für 689 asthmatische Anfälle. Bei 85 Asthmatikern, die Wildführ (1952) in Leipzig (Mitteldeutschland) untersuchte, entfielen 67,5% der Asthma-Anfälle auf meteorologisch gestörte Tage. Es handelte sich vorzugsweise um Durchzüge von Unstetigkeitsschichten, Fronten, insbesondere Warmfronten, und Okklusionen. Bei 6 besonders wetterempfindlichen Patienten waren es sogar 94,9% der Anfälle.

Amelung (Königstein im Taunus, Mittelrheingebiet) bezeichnet das Asthma bronchiale als ausgesprochen meteorotrope Krankheit und führt als auslösende Faktoren an: akute Witterungsveränderungen, brüsken Witterungswechsel, turbulente Vorgänge in der Atmosphäre, aber auch lokal-klimatische Einflüsse, wie plötzliche Zugluft oder starke Abkühlung. Während die Angaben von Daubert (1959), Brezowsky (1960) und Wildführ (1952) eine Steigerung in Warmluftkörpern fanden, sind die Ergebnisse für andere Gebiete abweichend. So sah Tromp (1957) nur bei Passage von Kaltfronten enge Beziehungen zum täglichen Anstieg der Asthma-Anfälle in Holland in der Nähe der Küste. – Quarles van Ufford (1958) beobachtete bei 1000 Bronchial-Asthmatikern in den Niederlanden bei 547 eine Wetterabhängigkeit, dabei reagierten 374 (68,4%) auf feuchtes Wetter und Nebel und 181 (33,1%) auf Nord- und Ostwind ungünstig. Für das Gebiet der Nordseeküste in Deutschland sind die allerdings nicht häufig auftretenden kontinentalen Hochdruckwetterlagen, insbesondere mit kalter, kontinental-polarer Luft, gefürchtet. Hänsche versucht eine Unterscheidung der Kinder nach Reaktionstypen, wobei die sympathikotonen auf zyklonale West- und Südwestwetterlagen mit gehäuften Beschwerden reagieren, die vagotonen dagegen auf kalte, kontinentale Wetterlagen. Letztere zeigten auch bei strahlungsreichen Hochdruckwetterlagen Neigung zur Verschlechterung. Diese Zusammenstellung von Wetterfaktoren findet auch Héraud (1948), der Sonnenschein und Föhn, also warm-trockene Luft, neben Sturm, Schneefall, kaltem Wetter und Feuchte verzeichnet.

Die Ergebnisse verschiedener Autoren weichen also nicht unerheblich voneinander ab. Das ist nicht Zufall oder gar ein Widerspruch, der den Wert der Beobachtungen einschränkt, sondern es handelt sich – wie ausdrücklich betont werden soll – um klimatische Unterschiede zwischen den einzelnen Beobachtungsgebieten. In ähnlicher Weise konnten Brezowsky und Menger (1959) am Beispiel der Meningitis epidemica unterschiedliche Einflüsse des Wetters in Süddeutschland (München), im Mittelrheingebiet (Mainz) und in Norddeutschland (Bremen) gegenüberstellen. In dem kühleren norddeutschen Gebiet wirken Kaltfronten intensiver, während diese im mittleren Abschnitt und in Süddeutschland an biotroper Wirkung verlieren.

Betrachtet man die etwas voneinander abweichenden Witterungsbedingungen in verschiedenen Gebieten Mitteleuropas, so ist eine Anfallshäufung vorzugsweise dann zu finden, wenn es zu einer wetterbedingten Verstärkung der klimatischen Eigentümlichkeit kommt. Statistische Ergebnisse können leicht dadurch beeinträchtigt werden, daß die einzelnen Menschen in ihrer Weise, untereinander aber verschieden, reagieren. Dadurch können die biotropen Einflüsse schwächer erscheinen als sie tatsächlich sind.

Die Jahre 1959 und 1960 stellten nahezu im ganzen Jahresablauf einen ungewöhnlichen Kontrast dar. Das Jahr 1959 war im norddeutschen Küstengebiet außerordentlich trocken und warm, das Jahr 1960 dagegen sehr feucht und kalt. Die Tabelle 1 zeigt eine Aufstellung der asthmatischen Beschwerden während der Behandlung im Kinderkrankenhaus Seehospiz auf der Nordseeinsel Norderney bei 834 Kindern.

Es ist zu erkennen, daß im warm-trockenen Jahre 1959 bei 172 Kindern (42,5%) und im kalt-feuchten Jahre 1960 bei 145 Kindern (33,8%) asthmatische Beschwerden oder Asthma-Anfälle auftraten. Der Verlauf war also im kalt-feuchten Jahre, in dem die zyklonalen Wetterlagen vorherrschten, günstiger. Die Differenzen in der Häufigkeit von Anfällen während der Behandlung an der Nordsee waren bei diesen Kindern also trotz der großen Gegensätze in der Witterung nicht sehr groß. Durch die Unterschiede in der individuellen Reaktionsweise der Kinder erfolgte statistisch betrachtet teilweise ein Ausgleich.

Besondere Häufungen von Asthma-Anfällen werden in bestimmten Jahreszeiten angegeben, doch in Abhängigkeit von klimatischen Verhältnissen unterschiedlich. So fand Daubert (1959) in Süddeutschland einen Anstieg bis zum Ende des Winters. Für 558 von 1000 Bronchial-Asthmatikern gibt Quarles van Ufford (1958) eine Abhängigkeit der Beschwerden von der Jahreszeit an, von denen der größte Anteil mit 204 auf die Monate August bis Oktober entfiel. Das entspricht den Darstellungen von Schook (1962), aus denen ein Gipfel von Juli bis Oktober zu entnehmen ist.

Der Verlauf einer Klimakur an der Nordsee war bei 1517 Kindern in drei Jahren relativ schlecht bei Beginn der Behandlung im Oktober, am schlechtesten bei Beginn im Dezember, dagegen am besten bei Beginn im Juni (Tabelle 2). Je kleiner die Kinder sind, desto mehr gilt diese Feststellung. Die Erfolge einer Klimakur, beurteilt nach dem Verlauf der Krankheit während der folgenden 12 Monate, sind aber bei Kindern über 10 Jahren am besten, wenn die Behandlung im Winter durchgeführt wurde.

Seit den Untersuchungen von Storm van Leeuwen wird den Pollen, Sporen und Schimmelpilzen besondere Beachtung geschenkt. Schook (1962) und Tromp (1957) stellten fest, daß sich während Perioden mit hoher Pollenhäufigkeit sehr wenig Asthma-Anfälle ereigneten und umgekehrt. Eine sehr deutliche, gegensin-

Tabelle 1. Anzahl der Kinder, die wegen eines Asthma bronchiale im Kinderkrankenhaus Seehospiz „Kaiserin Friedrich" in Norderney behandelt wurden

Häufigkeit der asthmatischen Beschwerden	1959	1960
Nie asthmatische Beschwerden, kein objektiver Befund	172	210
Nie asthmatische Beschwerden, aber objektiver Befund	61	74
Nur am Anfang asthmatische Beschwerden oder typischer Auskultationsbefund	41	24
Nur einmal oder zweimal während der Behandlungszeit Erscheinungen	63	61
Mehrfach leichte Beschwerden während der ersten Hälfte der Behandlungszeit	16	7
Mehrfach leichte Beschwerden während der ganzen Behandlungszeit	31	27
Starke oder häufige Beschwerden am Anfang der Behandlungszeit	12	14
Starke Beschwerden während der ganzen Behandlungszeit	6	10
Starke und anhaltende Beschwerden	2	—
Status asthmaticus	1	2
	405	429

nige Tendenz zeigte sich in den Jahren 1959 und 1960, also einmal in einem trokkenen und warmen, das andere Mal in einem sehr feuchten und kühlen Jahr. Die Asthma-Anfälle waren im Sommer 1959 relativ selten, die Schimmelpilzhäufigkeit in den Sommermonaten aber sehr hoch. Pollen und Sporen treten besonders in kontinentalen Luftkörpern nach regenarmer Periode im Sommer auf. Die örtliche Bodengestaltung und Anhäufung von Allergenen kann die Sensibilisierung disponierter Menschen fördern, die eigentliche Auslösung von Asthma-Anfällen erfolgt jedoch über eine Reizung des vegetativen Nervensystems durch aperiodisches Wettergeschehen und zwar mit Höhepunkt beim Übergang von advektiv warmen zu advektiv kaltem Wetter (Daubert, 1959).

Nicht nur Klima, Wetter und Jahreszeit spielen beim Asthma bronchiale eine Rolle und zwar im Sinne der Auslösung von Anfällen, sondern auch die Bodenbeschaffenheit ist bedeutungsvoll. Einerseits handelt es sich um die Form der

Tabelle 2 Beurteilung des Verlaufs einer durchschnittlich drei Monate langen Behandlung von 1715 Kindern mit Asthma bronchiale im Kinderkrankenhaus Seehospiz „Kaiserin Friedrich" in Norderney in den Jahren 1960–1962

Beginn der Behandlung im Monat	Sehr gut (günstiger Verlauf, Entlassung symptomfrei) %	Gut (leicht gestörter Verlauf, Entlassung symptomfrei) %	Befriedigend (stärker gestörter Verlauf, nicht ganz symptomfrei bei Entlassung) %	Nicht befriedigend %	Gesamtzahl Kinder
Januar	47	40	12	1	207
Februar	37	50	12	1	121
März	43	37	17	3	90
April	44	46	8	2	197
Mai	38	44	16	2	89
Juni	51	45	4	—	120
Juli	42	49	8	1	130
August	41	50	7	2	107
September	31	53	12	4	112
Oktober	26	61	10	3	147
November	45	44	10	1	145
Dezember	31	44	25	—	52
	41	47	10	2	1517

Bodenerhebungen, also die Orographie. Da der Asthmatiker sehr wetterempfindlich ist, sind geschützte Lagen auf der Lee-Seite von Gebirgen günstig, da sie die Wirkung zyklonaler Wettervorgänge abschwächen. Darüber hinaus ist die Beschaffenheit des Bodens weniger für die Auslösung als für die Häufigkeit des Asthmas bedeutsam. Von Knorre (1960) hat für den Bezirk Magdeburg in Mitteldeutschland die Häufigkeit von Bronchialasthma im Vergleich zur Bevölkerungszahl, den Asthmakataster festgestellt. Die Abweichungen in den einzelnen Kreisen sind ganz erheblich und bewegen sich zwischen 0,12‰ und 0,85‰. Dabei ist noch hervorzuheben, daß die Kreise mit den niedrigsten bzw. höchsten Zahlen benachbart liegen. Die relative Häufigkeit verhält sich also wie 1 : 7. Die grossen relativen Unterschiede sind auf die Bodenbeschaffenheit zurückzuführen. Gebiete mit relativ hohem Krankenstand an Asthma bronchiale fanden sich vorzugsweise bei nassen Böden, nämlich in Urstromtälern, Flußauen, bei Keuper und Liassenken, ferner im Bereich der Lössverbreitung. Wenig Asthma kam in etwas höher liegenden Gebieten mit Trockenböden, so bei Endmoränen, älteren Flußterassen und auf Sand, vor.

Alle diese Gesichtspunkte müssen bei der Behandlung des Asthma bronchiale berücksichtigt werden. In Deutschland spielt die *Klimatherapie* eine wichtige Rolle. Dabei sind drei verschiedene klimatische Gebiete zu unterscheiden. Waldreiche Mittelgebirgslagen (Amelung, 1960) bleiben durch verringerte Temperaturen meist frei von schwülen Tagen, weisen Luftreinheit auf und liegen im Winter oberhalb von Inversionen. Auf der Lee-Seite kommt die Abschwächung der Wettervorgänge hinzu. Es handelt sich hierbei um ein reines Schonklima. Im Hochgebirge werden Höhenlagen von 1000–1500 m in den Alpen bevorzugt (Roget *et al.*, 1958; Wolfer und Höchli, 1959). Allergenarmut ist in besonders günstiger Weise vorhanden, Pollen können je nach Jahreszeit eine Rolle spielen. Als drittes sind die Nordsee (Haeberlin und Goeters, 1954; Schultze, 1960) und die nach Nordwesten offenen Teile der Ostsee (Schmidt-Bonacker, 1960; Zenker, 1956, 1957) zu nennen. Gemeinsam für alle klimatherapeutisch wichtigen Gebiete ist die relative Sauberkeit der Luft als Schonfaktor. Die Anforderungen an den Organismus im Sinne einer Verbesserung der Haut- und Schleimhautfunktion sind aber sehr unterschiedlich. In niederen Lagen des Mittelgebirges kommt diese Wirkung kaum zustande, im Hochgebirge überwiegt ebenfalls die Schonung, wobei der Verlauf meist sehr günstig ist. Nach Wolfer und Höchli (1959) sind bei gleichen Autoren die Unterschiede zwischen störungsfreiem Verlauf während einer Klimakur im Hochgebirge und die Erfolge nach Rückkehr an den Heimatort recht groß. Jungmann (1962) hat kürzlich darauf hingewiesen, dass Misserfolge nicht nur auf einer Überdosierung klimatischer Reize, sondern auch auf einer zu starken Schonung beruhen können. Es ist also, soweit es der Organbefund zulässt, nach Möglichkeit eine Verbesserung der vegetativen Funktionen durch dosierte klimatische Reize anzustreben. An der See sind die Anforderungen an den Organismus durch die Wirkung des thermischen Komplexes, besonders des Windes, grösser. Eine gewisse Belastbarkeit muss daher gefordert werden, doch lässt sich durch sehr planvolle Dosierung die Therapie schonend einleiten. Die Verminderung der Anfälligkeit für fieberhafte Erkrankungen der Luftwege durch Verbesserung der Funktion der Vasomotoren der Haut gilt als wichtig.

Untersuchungen über den Einfluss des Kleinklimas bei Asthma bronchiale in Norderney (Menger, 1964a) haben durch Messung des Atemstosses mit dem Pneumometer „Minimus" gezeigt, dass die relative Verbesserung auf der See, bei Fahrt mit einem kleinen Schiff, sehr erheblich war und bei schwerem Asthma eine Steigerung um 54% ergab. Bei Asthmatikern mit mittelschweren Befunden betrug die Steigerung 33%, bei Nicht-Asthmatikern 7% gegenüber den Befunden im Hause. Die Reinheit der Luft und das maritime Aerosol wirken in vielen Fällen sehr schnell, was sich schon bei der Anfahrt mit der Bahn und insbesondere mit dem Schiff in auffälliger Weise zeigt, wie es auch durch Messung des Atemstosses experimentell bewiesen wurde. Spaziergänge am Strande während der Klimakur führen durch die kühle Luft zu einem Absinken der Schleimhauttemperaturen und einer Drosselung der Durchblutung, wie es als Reaktion auf die klimatischen Reize angegeben wird. Messungen der Schleimhauttemperaturen bei Asthmatikern ergaben starkes Absinken gegenüber Kindern, die an recidivierenden Krankheiten der Atemwege litten. Entsprechend muss die Dosierung der Klimareize vorsichtig erfolgen. Die reaktive Hyperaemie war in extremen Fällen aber deutlich, woraus die Funktionsverbesserung erkennbar wird. Die Ausnutzung des Kleinklimas zur Dosierung im Sinne einer Verstärkung oder Abschwächung der günstigen oder ungünstigen Wetterwirkung ist für den therapeutischen Erfolg entscheidend (Pfleiderer, 1961; Menger, 1964b). Ein Ziel der Behandlung ist die Verringerung der Wetterempfindlichkeit.

Eine Schwierigkeit der Beurteilung von Witterungseinflüssen auf den Ablauf von Asthma bronchiale zeigte sich deutlich bei den Klimakuren. Nord-Ost-Wetterlagen, wie sie Mitte Dezember 1962 auftraten, wirken im allgemeinen ungünstig, wie oben besprochen. Sind die Patienten aber schon einige Zeit in Seebad, kann bei fortschreitender Adaptation das sonst zu erwartende gehäufte Auftreten von asthmatischen Anfällen ausbleiben. Das Reizklima mit West-Wetterlagen hatte also bereits eine Verbesserung der Funktionslage im vegetativen Nervensystem herbeigeführt. — Eine Berücksichtigung der gesamten atmosphärischen Einwirkungen auf den Organismus kann eine wirksame Hilfe in der Behandlung des Asthma bronchiale sein, wobei die komplizierte Verknüpfung aller Einflüsse beachtet werden sollte.

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WIRKUNG DES HÖHENKLIMAS AUF ALLERGISCHE UND IMMUNITÄRE VORGÄNGE

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Abstract — The effect of altitude (1,400 m) on the clinical symptoms and the anaphylactic–hyperergic reactions after intracutaneous injection of allergens in allergic asthmatic patients is discussed and also the change of the tuberculin test reaction during the altitude treatment. A change in the response of the hormonal-vegetative system is discussed as an explanation for these effects. Numerous conversions from the negative to positive tuberculin reactions observed during the altitude cure after infection with tubercle bacillus or vaccination with BCG in cases which should have shown positive reactions are discussed in connection with the climatic effect on the reticulo-endothelial system, the rise of glutathion in the blood, the effect on the antibody formation and the allergic–hyperergic reactions.

Zusammenfassung — Die Wirkung des Höhenklimas (1,400 m) auf die klinischen Symptome und die anaphylaktisch-hyperergische Frühreaktion nach intracutaner Allergenapplikation beim allergischen Asthmatiker wird besprochen, ebenso die häufige Änderung der Reaktionsstärke des Tuberkulintestes während der Höhenklimakur. Als wahrscheinliche Ursache wird die klimabedingte Umstimmung vegetativ-hormonaler Reaktionsmechanismen erwähnt. Eine grössere Anzahl festgestellter Positivierungen im Verlaufe eines Kuraufenthaltes in der Höhe vorher negativer Tuberkulinreaktionen nach Primoinfektion und nach BCG-Impfung werden im Zusammenhang mit der Klimawirkung auf das RES, der Erhöhung des Glutathiongehaltes im Blut, deren Auswirkungen auf die immunologischen Vorgänge und der in der Folge entstehenden allergisch-hyperergischen Spätreaktionen diskutiert.

Résumé — L'effet du climat d'altitude (1,400 m.) sur les symptômes cliniques et la réaction anaphylactique-hyperérgique chez l'asthmatique allergique est discuté, ainsi que le changement fréquent de la réaction du test tuberculinique pendant une cure d'altitude. Comme cause probable de ces effets on considère la modification des mécanismes de réaction végétative-hormonale provoquée par le climat. Le fait d'un grand nombre de virages positifs, intervenus pendant une cure à l'altitude dans des cas de primoinfection ou après vaccination BCG, négatifs au commencement du séjour, est discuté en rapport de l'effet du climat sur le système réticulo-endothélial, de l'augmentation du titre de glutathion dans le sang, et de leurs effets sur les événements immunologiques et sur les réactions allergiques-hyperérgiques à la suite de ceux-ci.

Allergische und immunitäre Vorgänge beruhen auf identischen Mechanismen. Unabdingbares pathogenetisches Basalphänomen ist die Antigen-Antikörper-Reaktion. Die Wirkung dieser Reaktion bedingt im Organismus entweder Krankheit oder Schutz vor Krankheit. Das allergische Geschehen führt zu einem krankmachenden Zustand, das immuniologische dagegen schützt den Organismus vor der krankmachenden Noxe und deren Derivaten. Der allergische Sensibilisierungsprozess verläuft stumm, erst ein späterer, erneuter Kontakt mit dem Antigen verursacht im nun sensibilisierten Organismus Krankheitserscheinungen. Die Immunisierung hingegen entsteht nach der Infektion oder Impfung mit dem krankmachenden Erreger und nach Ablauf des entsprechenden Krankheitsgeschehens. Verschiedene immunitäre Reaktionen sind mit allergischen eng verbunden und die allergische Manifestation erweist die eingetretene und bestehende Immunisierung. Dies trifft auch für die BCG-Schutzimpfung zu. Die Tuberkulinallergie ist demnach das äusserlich sichtbare Ereignis des antiinfektiösen Schutzes, wobei der Stärkegrad der Tuberkulinallergie, nach bestehender Ansicht, vom Immunitätsgrad unabhängig ist.

Der günstige therapeutische Einfluss des Höhenklimas auf allergische Krankheiten, insbesondere auf das allergische Asthma bronchiale, ist bekannt. In einer früheren Arbeit wurden unsere diesbezüglichen Beobachtungen und Untersuchungen dargelegt. Es ergab sich, dass bei diesen Atopikern, experimentell und klinisch, trotz therapeutisch gutem und sehr gutem Erfolg keine direkte Wirkung des Höhenklimas auf die Antigen-Antikörper-Reaktion besteht, soweit eine solche mit dem Intracutantest als Früh- oder Sofortreaktion nachgewiesen werden kann. Im Gegenteil, bei erfolgreicher Kur im Höhenklima ist die reaktive Reizbeantwortung fast immer ausgeprägter als zu Beginn der Kur. Es wurde deshalb beim Asthmatiker in Verbindung mit oder als Folge der Allergisierung eine zentrale Fehlregulation angenommen, eine Bereitschaft zu Fehlleistungen des Systems Diencephalon-Hypophyse-Nebennierenrinde und der damit zusammenhängenden endokrinen und vegetativen Vorgänge, die zur Auslösung des initialen Reaktionskomplexes führen. Storck und Heim (1962) prüften die neurozirkulatorische Gesamtregulation bei Patienten mit Atopien und Ekzemen. Sie „fanden bei Patienten mit Atopien und rebellischen Kontaktekzemen während des ganzen Tages Änderungen, die einer vagotonen Einstellung des vegetativen Nervensystems ähnlich sind, wogegen Kontrollpersonen oder Patienten mit rasch abheilenden Kontaktekzemen während des Tages eine normo — bzw. sympatikotone Regulation nachahmen.“ Steinmann, Widmer und Kammer (1953) folgern aus ihren Untersuchungen über das Verhalten der Serumdiastase beim Bronchialasthma des Menschen, beim anaphylaktischen und beim Histaminschock des Meerschweichens: „Das Asthma wäre dann nicht als reines Organleiden aufzufassen, sondern als wichtigste Teilerscheinung einer allgemeinen neurovegetativen Dystonie auf allergischer Grundlage.“ Die bestehende „Reaktionsneurose“ wird durch das Höhenklima abgewandelt und umgestimmt, die überschiessende Reaktion auf die reizauslösenden Stoffe gemildert oder beseitigt. Durch das Höhenklima wird nicht der Basalmechanismus abgewandelt, hingegen durch Umstimmung die innere Bereitschaft zur asthmatischen Reaktion. Das aus der Auseinandersetzung zwischen Antigen-Antikörper entstehende Produkt vermag nicht mehr die Reizbeantwortung der Bronchien zu stimulieren, obschon die anaphylaktisch-allergische Hautreaktion deutlich zur Intensivierung und Verstärkung neigt. Es dürfte deshalb der anaphylaktisch-allergischen Sofortreaktion der Haut eine gewisse funktionelle Bedeutung und Eigenständigkeit zukommen, was auch für die hyperergisch-allergische Spätreaktion der Haut, die Tuberkulinreaktion zutrifft.

Sarvan *et al.* (1956) berichteten über Änderungen der Tuberkulinallergie bei 158 Patienten im Verlaufe eines Kuraufenthaltes an der adriatischen Küste. 67,1% davon zeigten keine, 32,9% eine deutliche Veränderung in der Stärke der Reaktion am Schlusse der Kur und zwar 22,1% eine stärkere und 10,8% eine schwächere. Zur Erklärung nahmen die Autoren Umstellungfaktoren der Adaptation und der Akklimatisation an das Meeresklima an. Eine derartige Kontrolle führten wir bei 402 tuberkulinpositiven Patienten anlässlich einer Kur in Höhenklima durch. Nach 4 Monaten Kuraufenthalt war bei 229 eine Veränderung der Tuberkulinreaktion feststellbar, 178 reagierten stärker und 51 schwächer.

Da der Ausfall der Tuberkulinallergie quantitativ nicht vom Immunitätsgrad abhängt, kann die Ursache der Reaktionsänderungen nur in der geänderten Reizbeantwortung und deshalb unterschiedlichen Funktion des Gewebssubstrates gesucht werden. Die Reaktion des Gewebes auf den Entzündungsreiz und damit auch die Intensität der Entzündungsreaktion hängt u.a. von der Reaktionslage des vegetativen Nervensystems ab (Heilmeyer und Kähler, 1962). Die klimatisch bedingte vegetativ-hormonale Abwandlung der Reaktionslage und deren Auswirkungen auf Gewebsreagibilität und Entzündungsreaktion ist als determinierender Faktor in Betracht zu ziehen.

Die Untersuchung der Frage der Beeinflussung durch das Höhenklima hyperergisch-allergischer Hautmanifestationen als Folge der Immunisierung nach Primoinfektion oder BCG-Impfung konnte an einem grösseren Beobachtungsgut durchgeführt werden und dürfte deshalb von Interesse sein.

In der Nachkriegszeit wurde bei einer grösseren Anzahl kriegsgeschädigter und Tbc.-gefährdeter Kinder, die zu einem Kuraufenthalt in der Höhe, 1400 m (Adelboden, Schweiz) weilten, beobachtet, dass die anfänglich negative Tuberkulinreaktion während des Aufenthaltes positiv wurde. Da die Patienten sich schon seit einiger Zeit in der Kurstation befanden, überraschte diese Feststellung. Trotz der sofort ergriffenen Massnahmen, wie strikte Trennung tuberkulinpositiver von den tuberkulinnegativen Kindern, Umgebungsuntersuchungen usw., die eine Infizierung auf der Kurstation mit Sicherheit ausschliessen liessen, wurden immer wieder neue positive Reagenten festgestellt, insgesamt 228.

Anlässlich der Unterbringung von Jugendlichen bis zu 18 Jahren aus Flüchtlings- und Konzentrationslagern, sowie Angehörigen solcher Insassen, kamen später 314 BCG-Geimpfte am selben Orte zur Betreuung. Von diesen reagierten beim Eintritt 142 negativ auf Tuberkulin, obwohl die Impfung 3–4 Monate zurücklag, bei einer kleinen Zahl etwas weniger oder etwas länger. Die Probe wurde vorerst mittels Moro–Patch durchgeführt und bei negativem Ergebnis 2 mal nach Mantoux in der Stärke bis zu 1 : 100 je nach Alter und Konstitution. Von den anfänglich 142 negativen Reagenten zeigten im Verlaufe des Kuraufenthaltes 63 eine spontane Konvertierung, ein Positivwerden der Reaktion.

Während die vorher angeführten Feststellungen sich einerseits auf Änderungen der anaphylaktisch-allergischen Erscheinungen des allergischen Asthma bronchiale, sowie der entsprechenden Hauttest-Reaktionen infolge Klimawirkung in der Höhe beziehen, anderseits auf Änderungen des bestehenden hyperergisch-allergischen Tuberkulin-Hauttests unter denselben Verhältnissen, so handelt es sich bei den letzteren beiden Kollektiven um:

1. Positivierung der zunächst negativen Tuberkulinreaktion trotz bestehender Primoinfektion;
2. Positivierung der zunächst negativen Tuberkulinreaktion trotz vorheriger BCG-Impfung.

In beiden Kollektiven aber wäre auf Grund normaler Immunisierungsvorgänge eine positive Tuberkulinreaktion schon vor Beginn des Kuraufenthaltes zu erwarten gewesen. Die Anzahl der Beobachtungen lässt sich kaum in die Variations- und Zufälligkeitsbreiten der Versager einordnen. Diese Feststellungen bedeuten deshalb, dass die nichtreagierenden, tuberkulinnegativen Patienten, welche infolgedessen des immunitären Schutzes gegen Tbc. entbehrten, während ihres Aufenthaltes in der Höhe „spontan" einen solchen entwickelten. Wie kann eine Erklärung dafür versucht werden?

Verschiedentlich ist schon auf Unterernährung und die damit zusammenhängenden Umstände in Verbindung mit einer Tuberkulinallergie hingewiesen worden, so von Kundratitz bei einem ähnlichen Beobachtungsgut. G. Wijsmüller hat kürzlich die Ergebnisse nach BCG-Impfung auf breitester Populationsbasis in Neu-Guinea mitgeteilt und die hohen Prozentzahlen negativer Tuberkulinreaktionen der ungenügenden und defizitären Ernährung und deren Folgen zugeschrieben, aber auch auf die Mitwirkung anderer, unbekannter Faktoren als mögliche Ursache hingewiesen. Baumann (1958) spricht von der Entwicklung einer negativen Allergie infolge Erschöpfung der Abwehrmechanismen bei mangelhafter und ungenügender Ernährung. Ob aber nach Behebung der Mangelernährung die Tuberkulinallergie sich in normaler Weise spontan entwickelt, ist noch kaum festgestellt worden, weshalb zur Erklärung unserer Ergebnisse wohl noch andere, auf der Klimawirkung beruhende Faktoren zu suchen sind. Schon vor einigen Jahren konnten Klinkhart und Regamey (1941) feststellen, dass im Tierversuch (Meerschweinchen) die Immunisierbarkeit gegen Diphtherietoxin in der Höhe deutlich grösser ist als in der Ebene und die Immunisierung im Hochgebirge — im Vergleich zur gleichartigen Vorbehandlung in der Ebene — die Bildung einer grösseren Antigenmenge auslöst. Der Antitoxintiter im Blut war bei den Hochlandtieren um 36% höher, und ebenso wurde die grössere Giftresistenz wahrscheinlich gemacht. Immunität und Allergie hängen mit der Tätigkeit des Retikulo-Endothelialen-Systems (RES) zusammen. Die Wirkung der Höhe auf das RES haben Müller und Cronheim (1932). Cronheim (1933), sowie Loewy und Cronheim (1933) im Davoser Institut und in Berlin untersucht. Durch Blockierung des RES gelang es, die Wirkung der Luftverdünnung ganz oder grösstenteils aufzuheben. Bei blockierten Ratten und Meerschweinchen sind unter Luftverdünnung in der Leber lediglich durch das Hungern bedingte Veränderungen nachweisbar, während die Luftverdünnung sonst weitergehende und spezielle Wirkungen auf den Leberstoffwechsel verursacht. Die Bedeutung des RES für das allergische und immunologische Geschehen ist bekannt. Der Reiz des Höhenklimas auf das RES und die dadurch bedingte Aktivierung ist deshalb wohl als wichtiger Faktor für sich einstellende immunologische Vorgänge in Betracht zu ziehen.

Die Vermehrung des Blutglutathiongehaltes in der Höhe von Deschwanden (1931); Delure und Vischer 1933) und die Beeinflussung der Sulfhydrilkörper in der Haut durch UV Strahlung (Asbeck, 1951; Wels, 1954) sind bei unseren Kollektivs, bei welchen zudem durch die besonderen Umstände eine wesentliche Verminderung des Blutglutathions vorhanden war, von ganz besonderer Bedeutung. Diese Vermehrung des Blutglutathions dürfte ganz wesentlich zur Antikörperbildung und deshalb zur Immunisierung geführt haben, da dem Glutathion in der aktiven Form die Beteiligung bei der Bildung der Antikörper zugeschrieben wird.

Zum Schluss sei noch ein Hinweis angedeutet. Letterer sagt: „Was wir als Allergie und allergische Krankheit schlechthin bezeichnen, ist einer bestimmten Reaktionsphase auf dem Entwicklungswege immunitärer Reaktionen zugehörig.“ Da durch das Höhenklima die immunitären Vorgänge gefördert werden, wären demnach verschiedene Wirkungen in dieser Sicht zu betrachten. Im Falle des Asthma bronchiale allergicum würde gegebenenfalls die gestörte bzw. inhibierte Regulation der zuvor gesetzten Reizbildung und der Weg in die krankhafte Reaktion, in die Immunopathie behoben, bei den erwähnten Primoinfektionen und BCG-Impfungen mit negativer Tuberkulinallergie die immunitäre Reaktion ermöglicht. Die positive intradermale Reaktion auf das entsprechende Antigen aber könnte als Zeichen der Abgestimmtheit des Funktionssystems gedeutet werden.

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RELATION ENTRE LES MALADIES ALLERGIQUES ET LA BIOMÉTÉOROLOGIE

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Abstract – In the study of the relationship between asthma and allergies of the respiratory tract and the meteorological and climatic conditions several considerations must be taken into account: selection of the most weather-sensitive patients; elimination of irrelevant factors; study of all meteorological parameters including air electricity separately and in combination with other factors and, finally, investigation of the pollens and various micro-climates.

Zusammenfassung – Das Studium von Beziehungen zwischen dem Asthma und den Allergien der Atemwege einerseits und den meteorologischen und klimatischen Erscheinungen andererseits erfordert die Berücksichtigung von mehreren Bedingungen: Auswahl der Kranken, die besonders wetterempfindlich sind, unter Ausschluß von Faktoren, die mit dem Gegenstand der Untersuchungen nicht in Beziehung stehen; Untersuchung von meteorologischen Parametern nicht nur der klassischen Art (Temperatur, Luftdruck, Strahlung), sondern auch Berücksichtigung der Luftelektrizität; Untersuchung der Gesamtwirkung der meteorologischen Erscheinungen und ihrer Veränderung; schließlich Untersuchung der Pollen und der Mikroklimate.

Résumé – L'étude de corrélations entre l'asthme et les allergies respiratoires d'une part, les phénomènes météorologiques et climatiques d'autre part, exige plusieurs conditions indispensables, méthodiquement analysées: — Sélection de malades présentant une sensibilité aux phénomènes météorologiques et climatiques, avec élimination des facteurs associés déclenchants non en rapport avec le sujet d'étude. Étude des paramètres météorologiques non seulement les paramètres classiques (température, pression, rayonnement) en insistant sur l'électricité atmosphérique; mais aussi étude des phénomènes météorologiques dans leur ensemble et dans leur évolution. Enfin, étude de la pollution et des microclimats.

1. LE POINT DE VUE MÉDICAL

Les maladies allergiques dans leurs rapports avec les problèmes météorologiques ou climatiques ont été étudiées au cours d'excellents exposés. Mais personne encore n'a parlé de ces maladies en se plaçant du *point de vue clinique*. Or, il s'agit là d'un problème essentiellement médical, *qui doit être résolu d'abord par les médecins*.

Notre point de vue français consiste tout d'abord à classer avec le maximum de précision, en utilisant les données cliniqueset biologiques, les malades allergiques qui présentent une sensibilité particulière aux phénomènes météorologiques ou climatiques.

Nous devons avant tout exiger un diagnostic exact avec la preuve réelle du facteur allergique causal et préciser la *hiérarchie de valeur étiologique* de l'allergène et des facteurs biométéorologiques.

Quelles maladies allergiques étudier en regard des effets météorologiques?:

- l'allergie cutanée,
- l'allergie alimentaire
- l'allergie du tractus respiratoire.

Il est évident que le facteur météorologique n'a rien à voir avec une dermite de contact.

Mais, dans l'urticaire par agent physique, le soleil et la lumière peuvent jouer un rôle et la manifestation clinique pourra dépendre ainsi de la saison, de la région, de l'intensité du rayonnement U.V.; nous savons sans difficulté mesurer ces facteurs.

L'eczéma atopique, l'oedème de Quincke ont souvent une relation avec l'un ou l'autre de ces facteurs. On sait que dans 50% des cas la guérison ou l'amélioration est apportée par un repos de trois semaines à la montagne, mais le mécanisme de cette action mériterait d'être étudié.

L'allergie alimentaire, l'allergie digestive sont difficiles à prouver. Il en est de même de la céphalée allergique, de la céphalée histaminique et de la migraine, mais on connait l'importance dans les céphalées du facteur météorologique qui joue un rôle déclenchant.

La place la plus importante doit être réservée à l'allergie du tractus respiratoire: rhinite, sinusite et asthme. Dans notre service parisien de l'hôpital Rothschild, nous avons pu établir que l'asthme est allergique dans 80% des cas: la preuve de l'allergie est fournie par l'histoire clinique, les tests cutanés et les tests de provocation (test de Tiffeneau à l'acétylcholine, tests de provocation par inhalation de l'allergène).

Mais l'allergie n'est jamais pure: la pollinose semble être le type des maladies allergiques pures et pourtant il y a plus de malades souffrant de pollinose dans les villes qu'à la campagne. Pourquoi? La pollution atmosphérique est un facteur irritant qui fixe les anticorps sur les cellules pituitaires ou bronchiques. Dès que la pollinisation commence, le malade présente les signes de rhume des foins ou d'asthme.

Pour les allergènes non saisonniers, comme la poussière de maison ou les moisissures, deux facteurs doivent être écartés avant d'étudier les paramètres météorologiques: l'infection et les éléments psycho-somatiques.

Avec la désensibilisation spécifique, les traitements anti-infectieux et psycho-somatiques appropriés, 50% des malades sont guéris, 25% améliorés, 25% ne retirent pas d'amélioration de ces traitements. Parmi ceux-ci nous trouvons l'allergie alimentaire dans 1% des cas, l'allergie microbienne dans 4%. Reste 20% des cas où l'étude des éléments allergiques infectieux et psychiques est négative.

C'est donc dans environ 50% des cas (de malades non guéris par les traitements précédents) que nous pouvons étudier particulièrement les facteurs météorologiques.

Mais dans cette éventualité (comme dans toutes les autres) il faut prendre le soin de faire un diagnostic différentiel de la cause déclenchante de la crise, autrement dit éliminer les facteurs associés déclenchants qui ne sont sûrement pas en rapport avec un paramètre météorologique:

- erreur alimentaire ou excès diététique
- troubles vésiculaire, hépatique ou intestinal
- stress émotif
- infection respiratoire intercurrente
- facteur hormonal tel que les règles
- effort musculaire
- prise d'un médicament même non allergisant.

Ce n'est donc qu'après un diagnostic de maladie allergique et un diagnostic causal différentiel bien établi, une fois éliminés les facteurs déclenchants associés qu'il sera possible de chercher une cause météorologique dans le déclenchement de l'asthme.

Il serait intéressant de dresser la carte d'une région donnée avec la fréquence des manifestations allergiques dans cette région. Une telle étude est difficile en France, en raison du grand nombre des micro-climats: ainsi dans le Bassin parisien existent des vallées au sol semi-perméable ou les asthmatiques sont nombreux; c'est particulièrement vrai pour la forêt de Senlis, au nord de Paris, qui est humide. Mais dans la forêt de Fontainebleau, forêt sèche, située à la même distance de Paris, où le sol est sablonneux, les cas d'asthme sont rares.

Pour connaître la bioclimatologie chez l'allergique, et surtout chez l'asthmatique, il faut donc aussi tenir compte de la géographie et de la géologie.

Conclusion

Notre société se doit d'établir une méthode commune d'examen méthodique et approfondi du malade allergique. Cette étude demande beaucoup de temps de la part du malade et du médecin, exige des observations rigoureuses relatant les circonstances d'apparition de la crise.

Ces points étant connus, il faudrait entreprendre sur les sujets sélectionnés selon les normes antérieurement définies (élimination des facteurs déclenchants associés) une étude des paramètres biométéorologiques déterminants ou déclenchants.

Alors seulement, on pourra dégager les éléments de corrélation avec les facteurs météorologiques.

Il faudrait enfin établir des statistiques portant sur un grand nombre de malades présentant une crise au même moment et au même endroit et, secondairement, dans un lieu différent avec un décalage de temps correspondant au même phénomène météorologique déclenchant.

2. LE POINT DE VUE BIOMÉTÉOROLOGIQUE

I. On a vu la complexité des problèmes cliniques que pose le choix des malades (spécialement des asthmatiques) pouvant faire l'objet d'une étude corrélative avec les phénomènes climatiques et météorologiques.

D'autres difficultés vont intervenir dans l'étude de ces facteurs météorologiques en raison de la complexité des phénomènes en cause et du danger d'interprétations superficielles ou abusives.

II. Dans l'analyse des paramètres météorologiques, nous retenons l'idée directrice suivante: les éléments constitutifs de l'environnement météorologique peuvent avoir un effet possible à différents niveaux:

(1) *Action au niveau de l'allergène:* dispersion du pollen ou des moisissures athmosphériques par le vent, rôle de la pluie ou de l'humidité . . ., action sur la constitution physico-chimique de l'allergène: ionisation, radiations, température?

(2) *Action au niveau du tissu ou de l'organe de choc:* par exemple, modification *directe* des conditions locales de la muqueuse respiratoire sous l'influence de la température, modification *indirecte* par des irritants mécaniques ou chimiques. C'est dire l'importance de l'étude de la pollution athmosphérique et du micro-climat d'un lieu de travail donné.

(3) Les phénomènes météorologiques peuvent avoir une *action générale directe* sur l'organisme en favorisant l'apparition d'une crise ou en aggravant l'évolutivité de la maladie.

Il peut s'agir d'une action sur un système donné, système neuro-végétatif ou appareil endocrinien. Certains faits sont simples: action du vent ou de la température sur des récepteurs ou des arcs réflexes connus, d'autres plus complexes, comme l'action de l'électricité athmosphérique, du champ magnétique, de la radio-activité.

(4) *Action générale indirecte* prédisposant à l'apparition des phénomènes allergiques ou asthmatiques:

– action a frigore favorisant un état infectieux qui lui-même déclenche des manifestations morbides

– Modification de l'électricité athmosphèrique créant un état d'hyperexitabilité sensorielle ou psychique, qui, chez l'asthmatique, peut déclencher une crise.

On voit ainsi les différentes hypothèses soulevées en ce qui concerne le niveau d'action de la pertubation électrique de l'athmosphère par exemple: action directe au niveau de l'allergène, action sur le tissu de choc, action directe ou à distance, sur un appareil, action indirecte par phénomène psychopathologique.

III. Il en résulte donc la nécessité d'envisager un grand nombre de paramètres météorologiques et il nous paraît actuellement difficile de faire un choix en ne se fiant qu'à quelques paramètres ou d'en éliminer à priori un ou plusieurs. Devant la complexité et l'inbrication de ces phénomènes, nous pensons qu'il faut les garder tous à des fins de confrontation. Il faut savoir cependant qu'un paramètre météorologique sans action spécifique peut n'être que le reflet d'un phénomène général ayant, lui, une action causale (modification de la température ambiante, correspondant au passage d'un front, par exemple).

IV. Quels sont les paramètres météoroclimatiques définissant l'environnement que nous choisissons?

(1) Les *paramètres* que nous appelerons *analytiques* ou *élémentaires*

(a) Evidemment les grands classiques météorologiques:

- température
- pression atmosphérique
- vent
- hygrométrie
- précipitations

— état de l'air

- durée d'insolation

(b) D'autres éléments plus complexes:

— La qualité du rayonnement:

rayonnement solaire direct, global, diffus, réfléchi, effectif, bilan radiatif
rayonnement U.V.
rayonnement infra-rouge

Il existe un bon appareillage de base pour ces mesures constitué par les thermopiles ou radiamètres, mais il peut être parfois difficile d'apprécier dans quelle ambiance radiative vit un individu donné.

— Le rayonnement cosmique peut présenter un intérêt, surtout en altitude. On a le choix entre les méthodes de mesure par boîtes bactériennes ou par éléments photographiques.

— La valeur et la qualité de *l'électricité atmosphérique* nous paraissent importantes. Les variations du champ électrique demeurent primordiales en tant que mécanismes causals, mais les phénomènes directement en rapport avec la physiopathologie se rapportent plutôt à l'ionisation de l'air et à sa conductibilité. Ces mesures sont très difficiles et l'on manque d'appareils précis, utilisables sans l'aide constante d'un électronicien.

— Citons encore d'autres paramètres comme la radio-activité atmosphérique et d'autres, plus mal connus, comme les variations du champ magnétique.

(2) Les *phénomènes* que nous appelerons *synthétiques*.

La synthèse d'un phénomène météorologique ne peut être faite que par des spécialistes de la météorologie qui réunissent différents renseignements sur un phénomène donné (par exemple, qualité d'un front, hauteur de la troposphère . . .) et en déduisent ses qualités propres, son déplacement etc. . . . . Une collaboration étroite doit donc être établie avec les organismes de météorologie.

(3) On doit aussi connaître les *phénomènes* que nous appelerons *dynamiques*, c'est-à-dire l'étude d'un phénomène donné en fonction du temps et de l'espace. Il peut s'agir d'un phénomène météorologique pur ou d'une modification de l'environnement par apport d'éléments anormaux pathogènes, allergisants ou irritants, ou de modification suivant le lieu ou le temps.

Nous faisons entrer dans ce cadre:

— l'étude de la pollution atmosphérique qui ne peut être faite que par des organismes habilités à cette recherche

— l'étude de la cartographie saisonnière, géographique et horaire de la pollinisation qui ne peut être faite que par des spécialistes qualifiés.

V. Au terme de cette enquête climato-météorologique ou plutôt de cette étude de l'environnement, on pourra définir de façon scientifique et chiffrée un climat loco-régional, voire un micro-climat selon le dispositif d'appareillage envisagé.

On tentera alors d'établir des corrélations avec les phénomènes pathologiques précédemment décrits.

Peut-on espérer par cette confrontation méthodique obtenir des relations de cause à effet entre le déclenchement d'un crise chez un allergique ou un asthmatique et la survenue de tel phénomène météorologique? Nous l'espérons, mais sans pouvoir encore ni donner de résultats, ni dire quels facteurs météorologiques semblent plus précisément responsables.

THE APPLICATION OF SIMULATED HIGH ALTITUDE CLIMATE IN A LOW-PRESSURE CLIMATIC CHAMBER FOR THE TREATMENT OF ASTHMA, BRONCHITIS AND OTHER DISEASES

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DURING a period of two years the physiological effects of high altitude (up to 3,000 m) have been daily applied therapeutically to a large number of patients in a specially constructed low-pressure climatic chamber at the University Medical Centre of Leiden, The Netherlands (Dept. of Internal Diseases). The favourable effects on asthmatic, bronchitic and allergic patients are discussed and new applications (e.g. rheumatic diseases) are suggested.

WEATHER AND ASTHMA IN JAPAN

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A Clinical mass survey was carried out on allergic diseases, mainly bronchial asthma and urticaria in the rural population. 400 subjects of both sexes were tested in a hill region near Tokyo and 488 of both sexes in an area near the sea in Shizuoka Prefecture. The incidence of asthma in each area was about 1.2 per cent and half of the recovered asthmatic patients had a positive family history of allergic diseases. The results of the clinical survey of 120 out-patients with bronchial asthma who visited our clinic during 1960 indicated that the frequency of asthmatic attacks was elevated in September, October and November during a year, and from evening to the early morning. The results of the statistical survey of 700 patients with asthma in the Allergic Clinic of Doai Memorial Hospital showed that 313 of the patients has asthma attacks in autumn, 101 in winter, 57 in spring and 63 in summer. At the change of the season 57 patients were worse and 38 patients also in the rainy season. Cold weather, weather conditions preceding rain or storm, common cold, over eating or stress were related to asthma attacks.

SMOG AND SO-CALLED "TOKYO-YOKOHAMA ASTHMA"

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To STUDY the so-called Tokyo-Yokohama Asthma a mass survey was carried out on 2219 persons in the Yokohama-Kawasaki area of Japan with 474 persons in a rural district as control. The previous medical history of 237 asthmatic out-patients was also studied. An increased incidence of cough with sputum and a significant decrease in vital capacity were found in the subjects in the Yokohama-Tokyo area, but there was no increase of shortness of breath. Studies of FEV/VC and bronchial-acetylcholine threshold were carried out and the results were compared with and verified by animal experiments. No definite evidence was obtained for the existence of "Tokyo-Yokohama Asthma".

BRONCHITIS, WEATHER AND CLIMATE

INFLUENCE OF WEATHER ON RESPIRATORY DISEASE*

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Abstract — The figures for application for admission through the Emergency Bed Service (E.B.S.) in London in 1955–1962 for respiratory disease were examined for their correlations with various meteorological factors after eliminating both the annual and seasonal trends. A correlation between respiratory disease and weather was found for males and females aged 45 to 64 years and 65 to 79 years and for females aged 15 to 44 years. Formally significant partial regression coefficients for the effect of atmospheric pollution on applications for admission through the E.B.S. of patients diagnosed as suffering from respiratory disease were found for males and females aged 45 to 64 and 65 to 79 years. Formally significant partial regression coefficients for the effect of temperature were also found for males aged 1 to 4, 5 to 14, and 15 to 44 years and for females aged 15 to 44 years. These findings were compared with previous work.

Zusammenfassung — Es wurde die Beziehung zwischen der Anzahl der Anmeldungen für die Aufnahme von Patienten mit Erkrankungen der Atmungsorgane beim Hilfsdienst für Spitalbetten (E. B. S.) in London in den Jahren 1955–1962 und den verschiedenen meteorologischen Faktoren untersucht, nachdem der Jahresgang der letzteren ausgeschaltet worden war. Eine Korrelation zwischen den Krankheiten der Atmungsorgane und dem Wetter wurde beim männlichen und weiblichen Geschlecht in den Altersstufen von 45–64 und 65–79 Jahren, beim weiblichen Geschlecht außerdem in den Altersstufen 15–44 Jahre festgestellt. Es wurden bemerkenswerte Koeffizienten für die Wirkung der atmosphärischen Verseuchung festgestellt, die zur Aufnahme durch den Hilfsdienst für Spitalbetten führten, und zwar bei Patienten männlichen und weiblichen Geschlechts in der Altersstufe von 45–64 und 65–79 Jahre, die an Krankheiten der Atmungsorgane litten. Besonders bemerkenswert sind die Koeffizienten, die durch Temperaturwechsel hervorgerufen wurden, in den Altersstufen 1–4, 5–14, 15–44 Jahre beim männlichen Geschlecht und bei dem weiblichen Geschlecht in der Altersstufe von 15–44 Jahren. Diese Beobachtungen wurden mit vorhergehenden Arbeiten verglichen.

Résumé — Le nombre des consultations pour maladies des voies respiratoires en vue de l'admission des patients dans les hôpitaux de Londres (E. B. S.) durant la période 1955 à 1962 a été compilé pour en extraire une corrélation avec de nombreux facteurs météoro-

* We wish to thank Commander J. R. E. Langworthy of the Emergency Bed Service for help in collecting the data and the Statistics Department at Rothamsted Experimental Station for help in analysing the data on their electronic computer.

logiques. Ceci ne fut toutefois fait qu'après élimination des fluctuations annuelles et saisonnières. On a trouvé une corrélation entre les maladies des voies respiratoires et le temps chez les hommes et les femmes des classes d'âge suivantes: 45 à 64 ans et 65 à 79 ans, ainsi que chez les femmes âgées de 15 à 44 ans. Les coefficients de corrélation entre les maladies des organes respiratoires et la pollution atmosphérique ont été significatifs pour les hommes et les femmes âgés de 45 à 64 ans, et de 65 à 79 ans. On a également trouvé de bonnes relations entre l'effet des variations de la température et les dites maladies chez les hommes de 1 à 4 ans, de 5 à 14 ans, de 15 à 44 ans et chez les femmes de 15 à 44 ans. Ces constatations sont comparées aux résultats de recherches antérieures.

THE object of these studies was to investigate the effects of certain meteorological variables on the incidence of respiratory disease using a statistical technique which eliminates large-scale seasonal and annual fluctuations.

There are two main reasons for this approach. In the first place there will always be a fairly close correlation between any two seasonally varying quantities even though there is no direct connection between them. Secondly, the large seasonal variation in the meteorological variables introduces very high correlations between them which can completely swamp their minor, short-term fluctuations. These latter fluctuations can throw much light on the independent effects of the individual variables. For example, the average temperature in August is always higher than the average temperature in January, and the relative humidity always lower, and to this extent temperature and relative humidity can hardly be considered to vary independently. But there can be warm, wet Augusts, or warm, dry ones and it is by comparison of warm and wet with warm and dry that the effects of humidity apart from temperature can be judged.

The method of analysis that we have used, though not perfect, seems to us to be more trustworthy than one in which the seasonal and yearly trends are not eliminated, and it is also more effective in separating the effects of the different meteorological variables. On the other hand, it may be less sensitive, and the fact that it shows no significant correlation between two variables does not necessarily imply that no correlation exists.

MATERIALS AND METHODS

Data for the occurrence of disease were derived from the Emergency Bed Service (E.B.S.) of the King Edward Hospital Fund for London.

The applications for admission of acutely ill patients through the E.B.S. have in the past been regarded as a good index of the incidence of respiratory disease in London (Bradley *et al.*, 1958, Abercrombie, 1953, 1956). This assumption has been based on the sharp increase in demand on the E.B.S. which regularly occurs at an early stage of an outbreak of respiratory disease, and particularly on the sensitive way in which this rise mimics the rise in deaths during a pollution fog episode (Martin and Bradley, 1960). Accordingly we decided to use the E.B.S. applications as our index of respiratory illness. Table 1 illustrates the data available for analysis.

Table 1. Data of E.B.S. Applications for Respiratory Disease in Greater London Available for Investigation

Age-group	Sex	Years
0–11 months	Male	1959–1962
	Female	
1–4 years	Male	1959–1962
	Female	
0–4 years	Male	1955–1962
	Female	
5–14 years	Male	
	Female	
15–44 years	Male	
	Female	
45–64 years	Male	
	Female	
65–79 years	Male	
	Female	

In order to see what the relationship was between the E.B.S. admissions and patients admitted to hospital in the London region, we made use of data provided by the General Register Office on the Hospital In-Patient Enquiry (H.I.P.E.) for Greater London for one year, 1958. These figures provide a diagnosis for a 1 in 10 sample of all patients discharged from hospital in Greater London. We found a close relationship in the rate of admissions (E.B.S.) and discharges (H.I.P.E.) for respiratory disease at all ages and in both sexes (Table 2).

The meteorological quantities examined were those recorded at Kew for mean daily barometric pressure (mb), mean daily temperature (°F), mean absolute humidity (mb), total rainfall (in.), total sun hours, and atmospheric pollution (as recorded by smoke concentration, mg/cm³) which are given in the Registrar

Table 2. Correlations of E.B.S. Applications for Greater London With Hospital In-Patient Enquiry Admissions by Sex and Month, 1958

Respiratory Disease (B 30–32)	Sex	r	P
	Male	0.93	0.001
	Female	0.92	0.001

General's weekly and annual summary. The calendar month was used as the unit of time in all calculations as it was not only the most convenient in abstracting records, but was also sufficiently long to smooth out some of the irregularities of weekly reporting, which are particularly noticeable when public holidays are present in a week.

Details of the method of analysis used are given by Snedecor (1956). Its essence is to fit a mathematical formula expressing the incidence of the disease under consideration in terms of the meteorological variables. The constants in this formula, which are estimated from the data, are called multiple-regression coefficients, and they summarize the effect of a unit change in the corresponding variable on the incidence of the disease, independently of the changes in the other variables. It is this property that makes the technique valuable in the present connection. By use of this method the effect of both months and years is eliminated. The values of these constants have been used to decide whether a given meteorological variable is effective in causing a change in the incidence of disease. If the corresponding regression coefficient does not differ significantly from zero, as tested by its standard error, then the data, so far as they go, do not provide evidence that there is any relation between the two. The size of the regression coefficients is unrelated to the strength of association and in this they differ from partial correlation coefficients.

The main disadvantages of the method are that it depends on relatively simple assumptions as to the mathematical relations between weather factors and disease, and that it takes no account of the fact that both disease and weather conditions tend to occur in "runs" so that values in neighbouring months tend to be correlated with one another.

The effect of the first drawback is usually to reduce the sensitivity of the method so that real effects may be missed. This implies that any effects found are correspondingly more firmly established.

The second disadvantage exaggerates the apparent significance of the results and may cause them to be taken as formally significant when they are not.

RESULTS

The total effect of the six meteorological variables on applications for admission through the E.B.S., London of patients diagnosed as suffering from respiratory disease is illustrated in Table 3. This gives the variance ratio (F) for each age and sex group of the multiple regression of the six weather variables on applications for admission. It may be seen that a formally significant effect is only seen amongst the older age-groups, in both sexes, at 45 to 64 years and 65 to 79 years, and in females at 15 to 44 years.

Table 3. Effect of Weather on Applications for Admission through the E.B.S., London, 1955–1962, of Patients Diagnosed as Suffering from Respiratory Disease, as Estimated by F Values, after Eliminating Effect of Month and Year

Age-group	Sex	Variance ratio (F)
0–11/12 months	Male	1.04
	Female	1.27
1–4 years	Male	1.36
	Female	0.49
5–14 years	Male	1.17
	Female	1.55
15–44 years	Male	1.68
	Female	2.00*
45–64 years	Male	3.34+
	Female	3.35*
65–79 years	Male	4.02+
	Female	2.48*

* Significant at 5% level
+ Significant at 1% level

In order to determine which of the meteorological variables affects applications for admission through the E.B.S., London of patients diagnosed as suffering from respiratory disease, the partial regression coefficients may be examined. Table 4

Table 4. Partial Regression Coefficients at Various Ages and their Standard Errors, of Applications for Admission through the E.B.S., London 1955–1962, of Patients Diagnosed as Suffering from Respiratory Disease, on Certain Meteorological Variables

Age-group	Sex	Partial regression coefficients (b ±S.E.)					
		Atmospheric pollution (smoke) concentration) mg/m³	Mean daily temperature (°F)	Mean absolute humidity (millibars)	Total rainfall (in.)	Mean daily barometric pressure (millibars)	Total sun hours
0-11/12 months	M	−1.60 ±1.42	−5.01 ±2.96	+ 7.21 ±10.27	+0.24 ±0.47	−0.01 ±0.50	+0.20 ±0.13
	F	−1.65 ±1.57	−1.80 ±3.26	− 9.21 ±11.32	+0.27 ±0.52	+0.65 ±0.56	−0.07 ±0.14
1-4 years	M	−0.28 ±0.82	−3.70* ±1.71	+ 9.21 ±5.92	−0.08 ±0.27	+0.01 ±0.29	0.00 ±0.02
	F	+0.63 ±1.14	−1.27 ±2.37	+ 2.40 ±8.21	−0.19 ±0.38	+0.22 ±0.40	0.00 ±0.10
5-14 years	M	+0.58 ±0.58	−3.01* ±1.43	+11.35* ±5.06	−0.30 ±0.21	−0.23 ±0.30	+0.06 ±0.07
	F	+0.25 ±0.64	−0.63 ±1.56	+ 1.45 ±5.52	−0.32 ±0.23	−0.22 ±0.33	−0.17* ±0.07
15-44 years	M	+0.39 ±0.51	−2.91* ±1.23	+ 8.33 ±4.38	−0.23 ±0.18	+0.10 ±0.26	0.00 ±0.06
	F	+0.35 ±0.47	−2.47* ±1.16	+ 5.06 ±4.10	−0.19 ±0.17	+0.14 ±0.25	−0.02 ±0.05
45-64 years	M	+1.31* ±0.52	−1.89 ±1.28	+ 2.46 ±4.53	· 0.09 ±0.19	+0.22 ±0.27	−0.04 ±0.06
	F	+1.35* ±0.49	−1.57 ±1.19	+ 3.58 ±4.21	−0.21 ±0.17	+0.18 ±0.25	−0.05 ±0.06
65-79 years	M	+1.40† ±0.52	−1.78 ±1.27	+ 1.41. ±4.49	+0.04 ±0.19	+0.32 ±0.27	−0.05 ±0.06
	F	+1.18* ±0.51	−0.29 ±1.25	− 1.76 ±4.41	−0.01 ±0.18	+0.35 ±0.27	−0.06 ±0.06

* Significant at 5% level, † Significant at 1% level

gives the partial regression coefficients and their standard errors for the various meteorological variables by age and sex group. It may be seen from these that formally significant regressions were found between applications for admission in those aged 45 to 64 and 65 to 79 years and atmospheric pollution, and inversely for mean daily temperature for males aged 1 to 4, 5 to 14, and 15 to 44 years and for females aged 15 to 44 years. A formally significant regression was also found for absolute humidity and applications for admission in males aged 5 to 14 years and total sun hours for females aged 5 to 14 years.

DISCUSSION

The evidence presented indicates that both atmospheric pollution and low temperature have an effect on the admission to London hospitals, particularly on those aged 45 years or more. The findings presented in this paper confirm those found by Holland *et al.* (1961).

Table 5. Partial Regression Coefficients at Various Ages and Their Standard Errors, of Applications for Admission through the E.B.S., London, 1955–1958, of Patients Diagnosed as Suffering from Respiratory Disease, on Certain Meteorological Variables

Age (years)	Partial regression coefficients (b ± S.E.)					
	Atmospheric pollution (smoke concentration) mg m³	Mean daily temperature (°F)	Mean absolute humidity (millibars)	Total Rainfall (in.)	Mean daily barometric pressure (millibars)	Total sun hours
0–4	−0.22 ±0.31	+0.068 ±0.085	−0.14 ±0.22	+0.14 ±0.14	−0.38 ±0.42	+0.65 ±0.49
5–14	−0.087 ±0.20	−0.035 ±0.055	+0.052 ±0.15	+0.019 ±0.09	+0.081 ±0.27	+0.16 ±0.32
15–64	−0.60* ±0.27	−0.15* ±0.07	+0.20 ±0.19	−0.13 ±0.12	−0.072 ±0.36	+0.23 ±0.42
65–	−0.66* ±0.23	−0.15* ±0.06	+0.20 ±0.17	−0.13 ±0.11	−0.25 ±0.32	−0.26 ±0.37

* significant at 5% level

In the previous paper only limited data of E.B.S. applications for admission for the years 1955–1958 was available. Table 5 illustrates the results then obtained (*N.B.* In the present data a log (Y+1) transformation of the applications for admission through the E.B.S. has been used so that the values of the partial regression coefficients are not the same.) It may be seen that formally significant regressions were also found between applications for admission in those aged 15 to 64 and 65 or more years and atmospheric pollution, and inversely for mean daily temperature. Holland *et al.* also showed (Table 6) a significant negative correlation with temperature for admission to station sick quarters with acute respiratory disease of recruits in two out of three Royal Air Force stations. In the permanent staff at these stations no single significant correlation was found between the occurrence of acute respiratory disease and temperature (Table 7). The

Table 6. Partial Regression Coefficients and their Standard Errors, of Admissions to Stations Sick Quarters, Hospital or Sick at Home of Male and Female Recruits at 4 Recruit-training Stations, on Mean Daily Temperature (°F) and Relative Humidity

Sex and Station	Partial regression coefficients (b ±S.E.)	
	Mean daily temperature (°F)	Relative humidity
Male:		
Hednesford	−1.77 ±1.53	+0.05 ±1.28
Bridgnorth	−4.69 ±2.09*	+0.03 ±1.86
Wilmslow	−8.06 ±4.03*	−4.06 ±3.63
Female:		
Wilmslow	−7.76 ±3.15*	−4.82 ±2.84

* significant at 5% level

Table 7. Partial Regression Coefficients and their Standard Errors, of Admissions to Station Sick Quarters, Hospital, or Sick at Home of Male and Female Permanent Staff at 4 Recruit-training Stations, on Mean Daily Temperature (°F) *and Relative Humidity*

Sex and Station	Partial regression coefficients (b ±S.E.)	
	Mean daily temperature (°F)	Relative humidity
Male		
Hednesford	−0.62 ±0.37	+0.19 ±0.31
Bridgnorth	−0.90 ±0.47	+0.40 ±0.45
Wilmslow	−0.03 ±0.47	+1.06 ±0.43*
Female		
Wilmslow	−0.95 ±1.12	+1.92 ±1.01

* significant at 5% level

pooled estimate of regression of both male and female permanent staff and recruits on temperature, however, was found to be significant.

The significance of these findings is difficult to judge. In view of the large number of regression coefficients examined it is to be expected that one or two might be significant at the 5 per cent point by chance alone. However, the close correspondence between the regression coefficients of E.B.S. applications for respiratory disease on atmospheric pollution in two different age-groups and in both sexes with the marked difference from the other age groups, leaves little doubt that a genuine relationship exists for these factors. Similar arguments can be applied to the effect of temperature, with the added confirmation of the R.A.F. findings. The significant regression of E.B.S. applications on absolute humidity in males aged 5 to 14 years and sun hours in females aged 5 to 14 years is less easy to explain. The particular values obtained differ markedly from those in other age-groups or in the other sex. It is perhaps noteworthy that a similar aberrant significant regression coefficient was found previously for the effect of relative humidity and admissions of permanent staff to one R.A.F. station sick quarters.

These findings confirm the ill-effects of low temperature and atmospheric pollution on mortality noted by others.

Farr (1885) drew particular attention to the effect of seasons and weather on mortality. He noted that the commonest causes of death in the cold months belonged to the pulmonary class and the cerebral diseases of the aged, but he did point out that many cases classified under apoplexy were probably due to "congestion of the lungs". The effect of atmospheric pollution on mortality has been recorded on numerous occasions both by Farr and by more recent workers such as Logan (1953) and Gore and Shaddick (1958). Reid (1958) reviewed the evidence of the effect of environmental factors in respiratory disease and noted particularly the effect of air pollution on respiratory disease, especially in older men. Boyd (1960), analysing mortality data in London and East Anglia, found respiratory mortality to be most closely associated with temperature and humidity in the two weeks immediately preceding death, but he was unable to separate the effects of humidity and temperature. The association was particularly noticeable in those aged 45 years or more and less distinct in the younger age-groups. He also found associations with pollution, particularly sulphur dioxide content. The more serious effects of urban fog appeared only to occur when fog was accompanied by very low temperatures, but his study differs from ours in that seasonal variations were not eliminated and he was dealing with mortality.

No effect of atmospheric pollution on respiratory disease in children is evident in our data, although the partial regression coefficients in the group aged 0 to 11 months resemble those of adults aged 45 years and over more than those of children aged 1 to 14 years, or young adults aged 15 to 44 years. Russell (1924, 1926) found an association between death from respiratory disease and fog in persons aged more than 55 years; but none in children.

From our previous data it was clear that a low temperature was associated with an increase in respiratory disease in adults apart from any effects of atmospheric pollution. In the present data formally significant effects are found in males aged 1 to 4, 5 to 14 and 15 to 44 years, and females aged 15 to 44 years. When low temperature and atmospheric pollution act together their effect is particularly clear, as in the 1952 "fog incident" when there was temperature inversion.

Young (1924) showed that in children there was an association between deaths from bronchitis and pneumonia and the mean temperature of the preceding week. Woods (1927) showed that in children there was an association between deaths from pneumonia and low temperature in those aged less than 40 years, but not in children aged less than 5 years. Payling Wright and Payling Wright (1945), however, analysing the data for 1923 to 1939, indicated that mortality from bronchopneumonia in both infants (aged 0 to 2 years) and the elderly (aged more than 55 years) rose rapidly when the mean daily temperature fell below 40° F. Simpson (1958) has also suggested that there is an association between the incidence of common colds and fall in temperature.

We have been unable to observe such a clear effect of temperature, but our study differs in that we have eliminated both the seasonal effect and short-term fluctuations. The apparent absence of an association between respiratory disease admissions in children and temperature may indicate that admission to hospital is not a reliable index of the incidence of respiratory disease in children in the community. Other factors, such as the social environment, probably play a very much bigger part in their admission than illness alone. Furthermore, low correlations will be masked by errors in the variables and by departure from linearity of regression, and short-term associations will tend to be missed by the monthly grouping of the figures.

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ACUTE RESPIRATORY DISEASE AND CLIMATE

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Abstract – Very little research has been done on the specific relationships between colds and climate and much of our knowledge must be extrapolated from investigations concerning the role of climatic conditions in the aetiology of more severe respiratory illnesses. This work is briefly reviewed and some results are presented of longitudinal studies of respiratory illness and its relation to climate in a nursery and in families in Sheffield, England, and in families in Trinidad, West Indies.

Zusammenfassung – Die spezifischen Beziehungen zwischen Erkältungen und Klima sind bisher nur wenig untersucht worden und viele unserer Kenntnisse müssen aus Arbeiten gefolgert werden, die die Rolle klimatischer Bedingungen für die Ätiologie schwererer Erkrankungen der Luftwege zum Gegenstand haben. Diese Untersuchungen werden kurz beschrieben und einige Ergebnisse längerer Studien über Erkrankungen der Luftwege und ihrer Beziehung zum Klima für ein Material an einer Pflegestation sowie in Familien in Sheffield, England, und Familien in Trinidad, Westindien, gezeigt.

Résumé – Il existe peu de recherches sur les relations spécifiques existant entre les refroidissements et le climat. La plupart de nos connaissances à ce sujet ont dû être extraites de travaux concernant le rôle que jouent les conditions climatiques sur l'étiologie des affections respiratoires les plus aigües. On décrit brièvement ici ces recherches ainsi que quelques résultats de longues études concernant les affections des voies respiratoires et de leur relation avec le climat. Pour ce faire, on s'est basé sur l'étude de patients d'un hôpital, ainsi que de familles de Sheffield (Angleterre) comparés à des familles habitant la Trinidad (Indes Occidentales).

In recent years, considerable advances have been made on the microbiological front in the investigation of the aetiology of respiratory disease. It has been recognized (Dingle, 1949) that bacteria play only a small part as aetiological agents, perhaps 1–2 per cent of all minor respiratory illnesses being attributable to them. At this moment, it seems probable that viruses are responsible for the majority of the seven or eight episodes of mild respiratory illness which we suffer each year. During the past decade, a multitude of hitherto unknown viruses have been recovered from individuals (usually infants in residential nurseries or personnel in military camps) with respiratory disease. Some of these, for example the rhinoviruses (Tyrrell *et al.*, 1960), are probably responsible for an appreciable amount of the colds we experience. Others, for example the parainfluenza viruses (Chanock *et al.*, 1958), are probably responsible only for a few colds in adults. In spite of these encouraging developments however, even the most competent workers, using apparently suitable tissue culture systems, can recover viruses from at most 15 per cent of colds occurring in the community. The problem presented by this gap may be evaded by assuming that the remaining colds are caused by viruses which we cannot at present recover. But no such evasion is possible when we consider the intriguing question "Why do we get more colds in the winter?"

The periodicity of disease and its relationship to climatic conditions have long been the subject of speculation. Thomas Sydenham wrote, in 1675, "For it so happens occasionally that the atmospheric influences may so coincide with an epidemic as to forward its development and to precipitate it, as it were, prematurely upon its victims." His speculation and many similar opinions expressed on the subject since early times were not put to the experimental touch until recently. Much of this experimental and observational work, however, must be treated with some reserve, insomuch as it is concerned with severe illness and death, rather than with the mild respiratory illness with which we are here concerned; nevertheless, it is likely that extrapolation is justified.

Low temperature (Russell, 1924, 1926; Young, 1924; Payling Wright and Payling Wright, 1945) and fog (Russell, 1924, 1926; Young, 1924) were then shown to be related to mortality from respiratory illness in adults and in children. A similar relation of air pollution to respiratory illness was observed in Los Angeles (Mills, 1957), and in Chicago (Mills, 1952) and in London (Logan, 1949). Van Loghem (1928), Simpson (1958), and Kingdon (1960) have shown a suggestive relationship between low relative humidity and respiratory morbidity.

Incidents such as the Meuse Valley (Roholm, 1937), Donora (Schrenk *et al.*, 1949) and the 1952 London fogs drew attention to the lethality of severe smoke-impregnated fogs. In the last of these incidents, a rise in mortality was evident on the first day of the fog, the highest figures being reached on the third and fourth days and the decline beginning on the fifth day (Logan, 1953). Three to four thousand excess deaths were attributable to this fog (Ministry of Health, 1954), a rise "as great as that during the worst week of the last cholera epidemic in 1866". At all ages, there were 2.6 times the number of deaths during the week of fog as during the preceding week, a higher proportion than that seen in previous severe fogs, in 1873 and 1880 (Martini 1953). This increase was mainly at the expense of older persons already suffering from chronic respiratory or cardiovascular disorders. Nevertheless, deaths in infants from bronchitis and pneumonia doubled and those in older children showed an increase of one third (Logan, 1953). In a general practice, the incidence of upper respiratory tract infection in all age groups trebled (Fry, 1953). In London at this time, observations at 116 stations suggested that there was a greater increase in deaths in the areas where there were high concentrations of smoke and sulphur dioxide (Ministry of Health, 1954; Wilkins, 1954). Local observations also suggested that the highest mortality rates were in districts near to sources of atmospheric pollution (Smithard, 1954).

Groups of chronic bronchitis patients have been observed by a number of workers. Positive correlations of death rates in these have been demonstrated with atmospheric sulphur dioxide (Pemberton and Goldberg, 1954), with consumption of domestic coal (Daly, 1954), with atmospheric sulphur dioxide and smoke (Waller and Lawther, 1955) and with atmospheric sulphur dioxide and temperature inversion (Roberts and Batey, 1957). Respiratory disease mortality has been shown (Boyd, 1960) to be correlated with the temperature and relative humidity of the two weeks immediately preceding; atmospheric sulphur dioxide and smoke showed no time trend with their correlations. Very low temperatures increased the lethality of the fogs. Reid (1958) observed positive correlations between bronchitis morbidity and frequency of fog and air pollution.

These observations have been supported by experimental work. Sulphur dioxide in high concentrations was found to be lethal to guinea-pigs. (Amdur *et al.*, 1952a) and to affect ciliary activity in rabbits (Cralley, 1942); its lethality was diminished by the presence of ammonia and accentuated significantly when the test was performed at 0° C (Pattle *et al.*, 1956). In man, the inhalation of sulphur dioxide in concentrations resembling those found in the 1952 London smog (i.e. 1–8 ppm) produced more rapid respiration and an increased pulse rate (Amdur *et al.*, 1953) and the tidal volume was diminished (Amdur *et al.*, 1952b). Lawther (1955) has not, however, confirmed these results.

The relationship between respiratory mortality and morbidity on the one hand and air pollution, low temperature and low relative humidity on the other seems clear. Little work has been done on the relationships of these climatic phenomena with minor respiratory illness and it may be of interest to examine such relationships in two studies which I made recently.

The first of these studies was carried out in a residential home for infants near Sheffield in the North Midland region of England. In this home lived some 15 to 20 children, aged from a few weeks up to five years old. I visited them twice weekly and kept a close clinical watch on them. Weekly throat swabs were taken from each child and I tested these for respiratory viruses. It was not possible to make measurements of atmospheric pollution, humidity and temperature at the nursery, but a number of stations were maintained by the Medical Research Council's group in Sheffield for the study of air pollution and I was kindly given data from the two nearest ones. Humidity and air temperature were measured at the Sheffield Museum.

The geographical situations of the nursery, the air sampling stations and their relation to the Sheffield industrial complex are given in Fig. 1: 1 represents the nursery, 2 and 3 the two M.R.C. sampling stations and 4 represents Sheffield Museum. To the west, south and south-east, the nursery looked onto open country with no sources of air pollution for many miles. To the north and north-east, there was the Sheffield industrial complex. The nursery and this industrial area were connected by the valley of the river Sheaf, which is bounded by hills rising to 1,000 ft on the west side and to 500 ft on the east. It is clear that, in the presence of a north or north-east wind, any air pollutants produced in Sheffield would be driven down the valley to the nursery. In the presence of a temperature inversion, this effect would be accentuated and the gutter formed by the valley would turn into a funnel. This north-east wind was uncommon and blew only on four consecutive days of 11–14 November on two successive days of 12–13 December and on 5 isolated days in November, January, February, March and April.

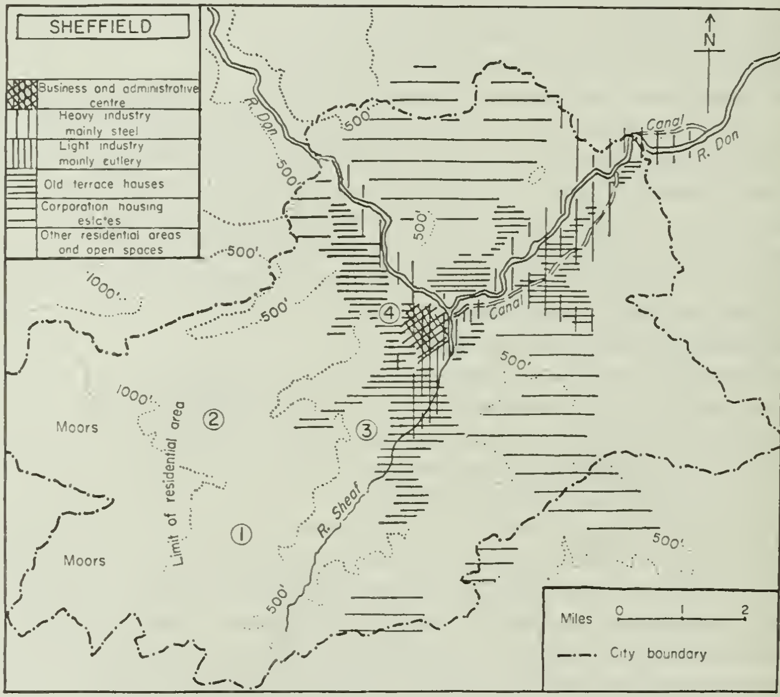

Fig. 1. The geographical situation of the residential nursery, the air sampling stations and the Sheffield industrial complex. 1. The residential nursery. 2 & 3. Medical Research Council air sampling stations. 4. Sheffield Museum.

Figure 2 shows the atmospheric sulphur dioxide as measured at the two sampling stations and the incidence of respiratory illness at the nursery, measured as illnesses person day. It sould be noted that the highest concentrations of sulphur dioxide recorded here were less than one fifth of those recorded in London during the 1952 smog disaster, i.e. 0.2 ppm as opposed to 1 to 8 ppm. Figure 3 shows the smoke concentration (at only one of the two stations; data from the other station followed the same trend), together with the incidence of respiratory illness at the nursery. From these figures, it will be seen that both smoke and sulphur dioxide concentrations followed the same trend over the period of the study. There were four peaks of respiratory illness incidence, in October, November, January and

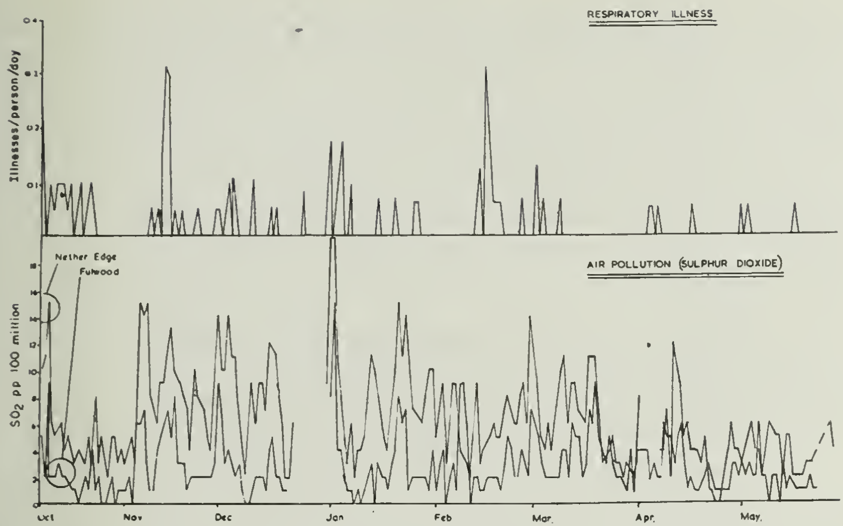

Fig. 2. Respiratory illness at the nursery and its relation to atmospheric sulphur dioxide.

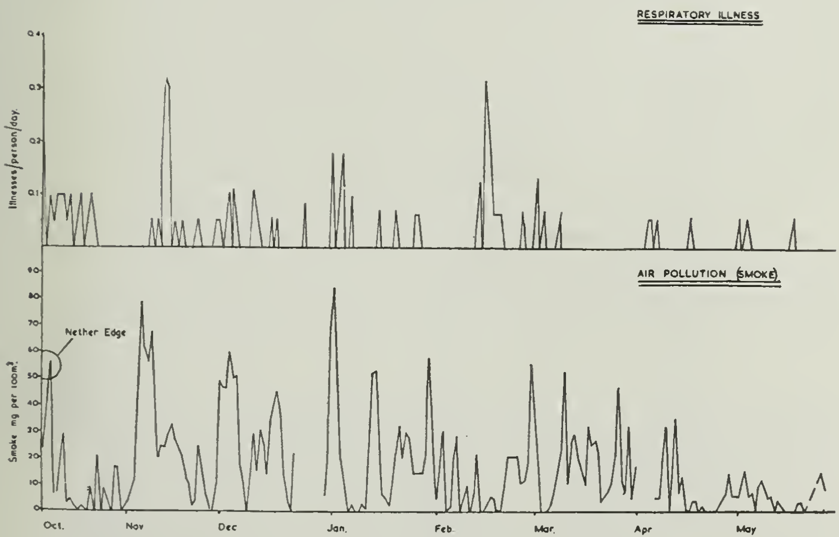

Fig. 3. Respiratory illness at the nursery and its relation to atmospheric smoke

NAME ________ BORN ________ NO. ________

ADDRESS ________ DR ________

.... DATE

DATE	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	
SORE THROAT	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
COLD IN HEAD	—	—	—	—	—	1	2	2	1	1	—	—	—	—	—	—	—	—	—	—	—	
COUGH	—	—	—	—	—	1	2	2	2	1	—	—	—	—	—	—	—	—	—	—	—	
HEADACHE	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
ACHE IN BACK OR LIMBS	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
FEVERISH	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	

Severity scale
- – Nil
- 1 Extremely mild
- 2 Mild
- 3 Moderate
- 4 Severe

PLEASE CHANGE THIS CARD ON

FIG. 4. Record card used in family survey

February. There were two peaks of relatively high concentration of smoke and sulphur dioxide, in November and January. The peak of air pollution in November preceded the peak in respiratory illness incidence by about six days; during four days of this period, there was a north-east wind and, in fact, there was a thick fog during two days with visibility limited to 200 yards. There were also slight falls in temperature and in relative humidity during the days associated with a high incidence of respiratory illness. In January, the correspondence of increased air pollution with increased incidence of respiratory illness was also close. At this time, there was again a thick fog, with visibility limited to 200 yards. There was a fall in temperature from 43° F to 28° F over 5 days and a fall in relative humidity from 81 to 65 per cent over 3 days.

The periods of increased incidence of respiratory illness in October and in February were not associated with corresponding peaks of air pollution. There were, however, falls in temperature and in relative humidity. These outbreaks were associated with proved infection with Influenza A virus, in October, and with Parainfluenza 3 virus, in February (Sutton, 1962; Sutton *et al.*, 1959).

In the second study, three groups of families were recruited. Two of these groups were in rural and in urban Trinidad, West Indies; the third group was in Sheffield. As frequent personal visiting was impracticable, record cards of the Hope Simpson type (Fig. 4) were used, these being collected at three-weekly intervals, either personally or by post. These cards are of considerable use in epidemiological work, giving results comparable with frequent personal visiting, although there is less detail. In Trinidad, 43 families, with an average size of 6.8 individuals each, were recruited; over 16 months, they recorded on their cards an experience of 177 person/years. In England, there were 14 families, with an average size of 4.2 individuals, and they recorded on their cards an experience of 56.8 person/years. The illnesses recorded on the cards were analysed, attention being paid to respiratory illnesses. These were defined as those recorded illnesses reported as including sore throat, cold in head or cough with or without any other symptoms.

Monthly rainfall data were obtained, through the kindness of the Trinidad Government, from 32 stations in East and West Trinidad; these were averaged to give a composite figure for the whole island. Estimations of humidity were not available. In Sheffield, rainfall data were available through the kindness of the City Museum authorities.

The periodicity of respiratory illness in England is shown in Fig. 5, where the expected peak is seen during the winter months, October to March. The periodicity in Trinidad differed considerably from this, the periods of increased incidence of respiratory illness (Fig. 6) being in June 1961 and June 1962. This periodicity held for both rural and urban groups of Trinidadian families. In Fig. 7, rainfall and the incidence of respiratory illness in Trinidad are plotted with the same ordinates. There is clearly a close correlation between the two. In Fig. 8, the same data are given for the Sheffield group of families. A similar, less close correlation is visible.

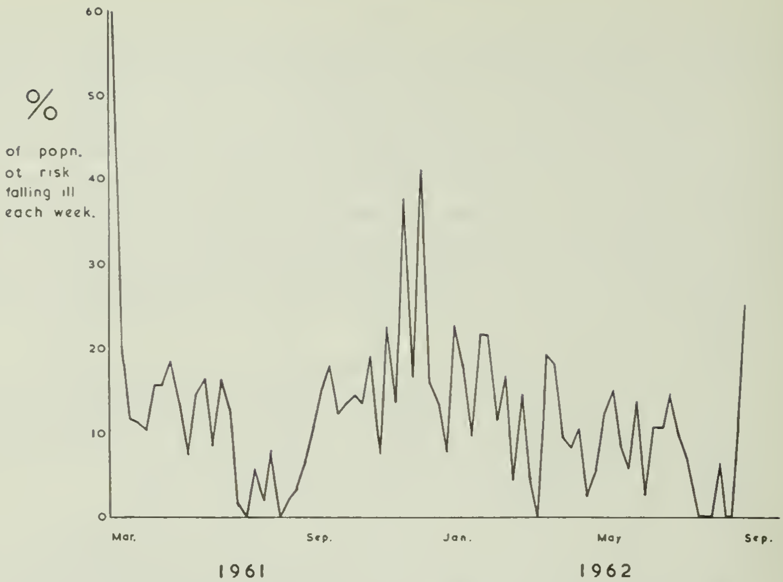

FIG. 5. Periodicity of respiratory illness in Sheffield families 1961–1962

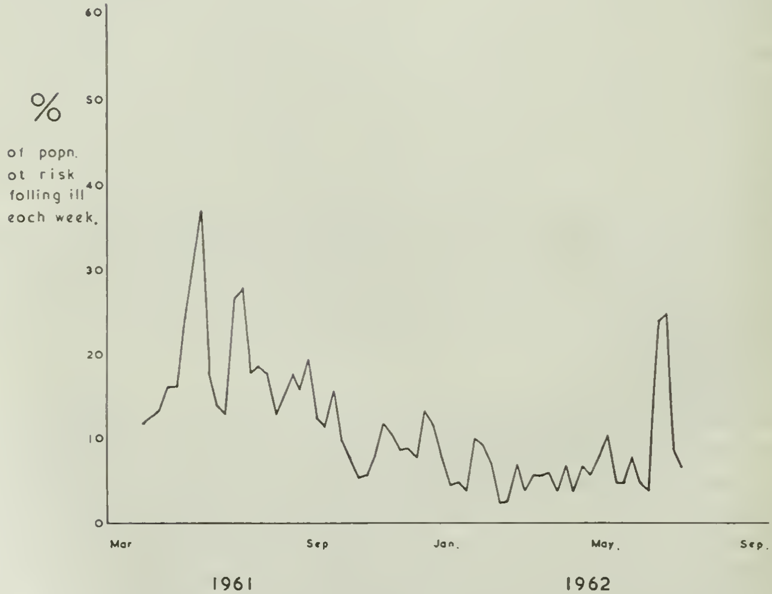

FIG. 6. Periodicity of respiratory illness in Trinidad families 1961–1962

Consideration of the literature on respiratory disease and its relation to climatic factors suggests that low temperature, low relative humidity, fog and air pollution are all pertinent factors. Viruses and, to a lesser extent, bacteria also

FIG. 7. Rainfall and respiratory illness incidence in Trinidad 1961–1962

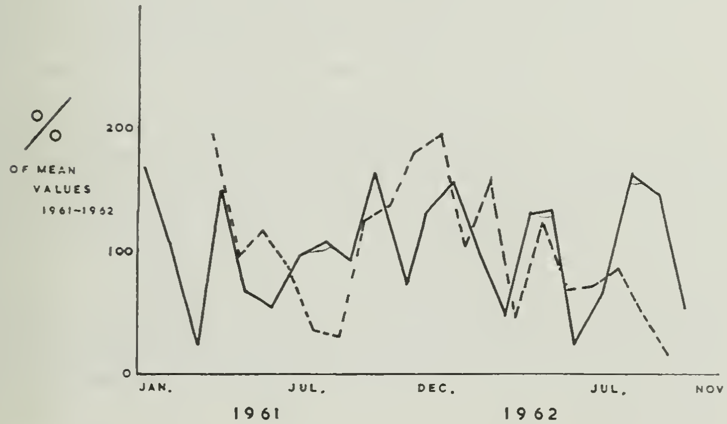

FIG. 8. Rainfall and respiratory illness incidence in Sheffield 1961–1962

play very prominent roles in the aetiology of respiratory disease. We must clearly attempt a synthesis of these widely differing factors before we can arrive at a clear understanding of the mechanisms behind the characteristic periodicity of our respiratory illnesses. Respiratory viruses are present in the community throughout the year and, with the exception of the influenza viruses, do not seem to change their antigenic character greatly as the seasons go by: it is therefore difficult to attribute periodicity to changes in the infecting viruses. Climatic factors do fluctuate, however, and it is possible that they exert their effect on the incidence of respiratory disease in two ways. Firstly, the microclimate of each individual may be altered, in particular the microclimate of the nasal mucosa and upper respiratory tract. Air pollution, including atmospheric sulphur dioxide and smoke concentrations will influence this, as will changes in humidity. The fluctuation in respiratory illness incidence in the Sheffield nursery as the degree of air pollution varied is in accordance with this. The population of the nursery was relatively constant over the period of the study and the degree of crowding together constant and these factors may therefore be ignored. It appears probable that sulphur dioxide and smoke, possibly potentiated in conditions of low relative humidity and low temperature, damage the surface epithelium of the upper respiratory tract, especially the nasal mucosa, and either permit infection with respiratory viruses or initiate a non-infective allergic rhinitis.

Air pollution in Trinidad, however, was completely negligible and the temperature over the year varied little and yet considerable periodicity in respiratory disease was observed. This periodicity followed the rainfall and a similar, although less marked, correlation was seen in Sheffield families observed simultaneously. A second method of interaction between climate and infectious respiratory disease seems to be operative here. The rainfall in Trinidad is heavy and limited to certain months in the year; it also has the effect of driving people from the streets and beaches into their own homes and so increases the amount of crowding together and hence the chances of susceptibles being exposed to infection by viruses. That such an indefinite factor as an increase in the degree of social overcrowding may be of significance in the spread of airborne epidemic infections has been shown experimentally by Andrewes and Allison (1961) using chicks infected with NDV virus. In their experiments, healthy chicks separated from infected ones by a low glass partition became infected as they crowded close to their fellows whom they could see, whereas when separated by a metal partition of the same dimensions as the glass one, no crowding and no spread of infection occurred.

In the English families, the periodicity of respiratory disease was similarly associated with that of the rainfall, but to a lesser degree; here temperature variations and fluctuations in air pollution, although not specifically seasonal, no doubt influence the relationship.

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LUNGENKRANKHEITEN IN BEZIEHUNG ZUM KLIMA

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Mit der zunehmenden längeren Lebensdauer und der Beherrschung der früher oft lebensbedrohenden katarrhalischen Komplikationen bei Erkrankungen der oberen Atmungswege und der Lungen ist von Jahr zu Jahr mit einer erheblichen Zunahme des Emphysems zu rechnen. Viele scheinbar echte Herzkranke haben keine primäre sondern eine sekundäre Herzerkrankung (W. Hadorn). Sie leiden an einem Cor pulmonale (C.p.) infolge Lungenemphysems. Zur Auswahl des Heilklimas beim Emphysem sind entscheidend: (1) die Form des Emphysems, (2) die Herzleistungsfähigkeit des Kranken und (3) das Fehlen oder Vorliegen ernsthafter Lungenfunktionsstörungen. Die Angaben des klimatologischen Schrifttums über das Emphysem sind bisher recht dürftig. Bisweilen vertragen Patienten mit schwerem Emphysem trotz des erniedrigten Sauerstoffpartialdrucks geschützte Hanglagen der Hochgebirgstäler. Dagegen sah Vortragender Emphysematiker, bei denen bei Verlegung schon in die submontanen Stufen des Mittelgebirges (etwa 300 bis 500 m) eine plötzliche, schwere, langanhaltende Verschlechterung des Krankheitsbildes eintrat (akutes C.p). Das C.p. als Folge des obstruktiven Emphysems führt zu einer progrendienten schlechteren Belüftung der Lunge. Da die Sauerstoffmangeltoleranz ebenfalls mit zunehmender Höhe über dem Meeresspiegel abnimmt, vertragen solche Patienten mit C.p. schon geringe Meereshöhen schlecht. Nach M a t t h e s würde ein Patient, der 88% arterielle Sauerstoffsättigung in Meereshöhe hat, in 2000 m Höhe eine Sauerstoffsättigung von nur 77% haben, die ein Gesunder erst bei 5000 m erreicht. Sicherlich haben Altersemphysematiker oft nur eine geringe O_2-Sättigung, aber diese kann in Höhen bis 1200 m durch verstärkte Atmung und eine geringe Erhöhung des Atemvolumens kompensiert werden. Aber leichte Diffusionsstörungen können durch körperliche Belastungen verschlimmert werden. Jeder Emphysematiker muß individuell hinsichtlich seiner klimatischen Belastbarkeit studiert werden.

CHRONIC BRONCHITIS AND AIR POLLUTION

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The U.K. has the highest death rate from bronchitis of any industrialised country. In the last ten years research has been directed to finding the causes. Related factors are: age, sex, smoking (especially of cigarettes), industrial dust and fume exposure, and socio-economic variables. The multiplicity of factors, the lack of agreement about diagnosis in its early stages, and the slow progression of the disease, also the paucity of past atmospheric pollution measurements, makes it impossible to express quantitatively the relative importance of general air pollution and other meteorological variables compared with the other factors. Evidence of association between air pollution and meteorological variables with deaths and sickness from bronchitis, will be presented for U.K. and some other countries. A plea is made for better standardisation of methods for obtaining relevant medical and environmental indices. Examples of recent international epidemiological studies, using such methods, will be given.

DIFFERENCE IN METEOROTROPIC BEHAVIOUR BETWEEN SUBJECTS SUFFERING FROM BRONCHIAL ASTHMA AND ASTHMATIC BRONCHITIS

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DURING a 10-year period (1953–1963) data have been collected in the western part of the Netherlands (at Leiden and Hilversum) on the effect of different meteorological conditions on patients suffering from bronchial asthma and bronchitic asthma; both adults and children (10 to 18 years of age). The following differences were observed: (1) Fog has little or no effect on patients suffering from bronchial asthma, contrary to the bronchitic patients. In this latter group complaints usually increase rapidly after the slightest increase in foggy conditions of the atmosphere, particularly if the patient is living in a heavily polluted area. (2) During the waterbath test (developed by the author) the warming curve of the patient remains horizontal for a considerable time whereas the curve of the bronchitic patient shows a more rapid (although also irregular) rise. However, both curves remain below the initial temperature level. As explained in previous publications this suggests a difference in thermoregulation efficiency. (3) As a result of this difference, a patient suffering from bronchial asthma is usually more affected by sudden cooling conditions than a bronchitic patient.

CLIMATE, WEATHER AND SEASON IN RELATION TO RESPIRATORY INFECTION

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Abstract — Respiratory infections are not necessarily commoner but are certainly more troublesome, more in evidence, in winter months and in cooler climates. Seasonal and climatic differences are less likely to be due to differences in spread of infection or to differences in virulence of organisms than to effects of host-resistance. There may be a unifying principle to be discovered or the answer may be a complex one, not necessarily the same for all pathogenic agents.

Zusammenfassung — Infekte der Luftwege sind nicht notwendigerweise verbreiteter, aber bestimmt quälender und augenfälliger in Wintermonaten und in kälteren Klimaten. Jahreszeitliche und klimatische Unterschiede kommen weniger durch Unterschiede in der Verbreitung der Infekte oder durch Unterschiede in der Virulenz von Erregern zustande, als durch die Wirkung der Widerstandsfähigkeit des Wirtsorganismus. Ob nun ein einheitliches Prinzip oder eine komplexe Antwort auf diese Problem gefunden werden mag, sie wird nicht notwendigerweise für alle pathogenetischen Vorgänge dieselbe sein.

Résumé — Les affections des voies respiratoires ne sont pas nécessairement plus répandues, mais certainement plus visibles et surtout plus fortement ressenties durant les mois d'hiver ainsi que dans les climats froids. Les différences saisonnières et climatiques se remarquent moins par des modifications de l'extension des agents pathogènes ou de la virulence de ceux-ci que par des modifications de la résistance de l'hôte à leurs attaques. La réponse au problème ainsi posé sera peut-être un principe unique ou complexe, mais elle ne sera pas nécessairement valable pour tous les agents infectieux.

THE subject we are to discuss is a large one. Climate, weather and season are important and complex variables. Respiratory infections may be caused by many kinds of viruses. I shall not be discussing streptococci, meningococci and other bacteria whose behaviour is rather different. We have Influenza A virus which comes in epidemic waves, often two years apart. Influenza B virus rarely causes such widespread outbreaks and sometimes confines itself to attacking closed communities such as boarding schools. Adenoviruses also cause trouble rather infrequently in the population generally but are a curse when recruits to the services are first gathered together. The same applies to the Coe virus, now called Coxsackie A21. On the other hand the parainfluenza viruses 1, 2 and 3, are noteworthy for causing minor respiratory infections amongst small children. The respiratory syncytial virus does this too, often with bronchiolitis and bronchopneumonia, but may also produce re-infection of older people and then cause symptoms of common colds. Finally the lately recognized rhinoviruses, of many — perhaps 40 or more — different serological types, are the most important causative agents known of common colds in adults (Tyrrell *et al.*, 1960). We have studied these for some years at the Common Cold Research Unit at Salisbury, using human volunteers. Finally there are still many respiratory infections of which the cause is unknown. All of these things afflict us more in winter than in summer, in temperate more than in tropical climates. Here again there are differences which are hard to explain. Influenza outbreaks in the northern hemisphere come most often about the New Year; yet prevalence of common colds shows a sharp peak at the first onset of cold weather in September and October with later peaks at the New Year and often again in March. I have referred in earlier discussions of this subject to a "winter-factor" affecting prevalence of respiratory disease. I do not know what it is. If there is a single factor affecting in rather different ways all these respiratory infections, our task becomes easier. The solution may, however, be very complicated. Nevertheless, until it is proved to be complex I feel we should search for a unifying concept.

CHILLING AND COLDS

One must mention in passing the belief that chilling of the individual precipitates a cold. Very many people believe this. Carefully conducted experiments in Britain and the U.S.A. have failed to substantiate the belief. It may nevertheless be true: it may be that only in individuals caught at a particular state of host-parasite equilibrium does chilling have this effect and perhaps a virus is activated in such people and then spreads to others. This idea would appeal to me more if someone could actually demonstrate this alleged effect of cold: statistics are so much more helpful than folk-lore. We shall be hearing from Dr. Hope Simpson on the matter of whether colds are "caught" by close contacts of cold-sufferers or whether activation of latent infection is more important. My own belief is that both things are involved. I have read a suggestion that summer colds are more apt to be sporadic and less likely to affect several members of a family than are colds in the winter (Lederer, 1928).

COLDS IN DIFFERENT CLIMATES

There is general agreement that colds soon become few and then disappear in small isolated communities. Such small communities have been observed particularly amongst polar explorers or other units cut off by arctic weather. I have little doubt that the conventional explanation is correct. Such a small community soon eliminates, or becomes resistant to, the limited number of respiratory pathogens circulating in that unit. It is probable, however, that some non-specific element of resistance becomes less effective in such a community, for there are frequently bad outbreaks of colds at the end of a period of relative isolation when contact is re-established with the outside world. Recent evidence that rhinoviruses are of many different serological types makes all this easier to understand. At least we have good evidence that chilling by itself does not cause colds.

People living in the tropics give rather different accounts of incidence of colds in warm countries. Most agree that these are less prevalent than with us in Europe; they may, in the East, be worse at monsoon seasons rather than being associated with temperature changes. The impression I get is that while such infections may be widespread in the tropics, they tend to be relatively mild. It has also been reported to me that on ships travelling home from the East, an outbreak of colds among passengers is apt to occur when passing from hot weather in the Red Sea to cooler waters further north. Dare one, as far as prevalence of respiratory disease is concerned, equate the European or North American summer with the all-the-year warmth of the tropics, or the drop in temperature in the northward travelling passenger-ship with the chills of autumn in temperate climes?

CLIMATE AND INFLUENZA

Outbreaks of influenza due to influenza virus A undoubtedly occur in tropical countries, but there the seasonal influence is not very noteworthy. In the Caribbean, influenza may occur at any time of year. When a novel antigenic type of influenza appears as in 1957 and presumably in 1918, the relative immunity of the tropics is no longer seen. The 1918 pandemic killed its millions in India. An unexpected phenomenon occurred in 1957. The new A2 or Asian virus, originating in China, spread rapidly round the tropical regions of the world, affecting countries with both arid and humid climates. Within a short time large numbers of the populations were attacked, and then the wave passed and was gone. Both in North America and in Europe the virus was introduced early in the summer, yet outbreaks were only in rather small foci; no general spread occurred for some time. Only when the weather became cooler around September did the epidemic break in full force. It was as if some controlling influence, possibly a non-specific immunity, not manifest in the tropics, delayed the attack, or the virus. And this although the strain was antigenically so new that populations had no specific immunity against it.

WEATHER AND RESPIRATORY INFECTION

Many attempts have been made to relate respiratory disease prevalence to temperature, humidity and other meteorological factors; they have met but little success. The only suggestive data concern not absolute values, but sudden changes. Such change often precedes an outbreak of colds by a few days.

Much of what I have so far mentioned rests on casual uncontrolled observations. One could speak with much more confidence of the effects of climate, weather and season, if observers in a few places scattered over the world, in places with very different climates, could collect data on a standardized plan. The data should cover clinical types of respiratory illness and their prevalence together with meteorological changes, and any important movements of populations. If to these data could be added information from the laboratory as to the agent concerned, they would be far more valuable. I am hopeful that WHO influenza laboratories, of which there are over 60 around the world, might form the basis of such a data-collecting plan.

POSSIBLE REASONS FOR SEASONAL DIFFERENCES: FACTORS AFFECTING SPREAD

One can invent all sorts of hypotheses as to why colds and such infections should prevail in winter, and these hypotheses may be placed in one of three categories. The infecting agent may get from person to person more easily in summer. The agent may undergo changes in virulence according to season. The resistance of the host may vary.

First, changes in ease of transmission. The virus or bacterium might survive more readily outside the body under conditions of greater cold, or lower relative humidity. Hemmes, Winkler and Kool (1960) showed that the virus of influenza, a winter infection, survived best when relative humidity was low, as it is in houses in winter. Poliomyelitis virus, on the other hand, survived best when relative humidity was rather higher, as it is in the summer and autumn, when polio is commoner. Rhinoviruses, however, the most important causes of colds that we know of, unfortunately fail to fit in with these notions. They are taxonomically related to Poliomyelitis virus and, like it, do not live so long when relative humidity is low. Yet they are winter infections, and their behaviour therefore fails to support Hemmes' suggestions.

A factor very little considered is light, to which many viruses are rather susceptible. Much evidence, however, suggests that cold viruses, at least, pass from one subject to another very rapidly: the direct hit from a shot-out droplet seems more important than the droplet nucleus floating for some time in the air. It is thus rather unlikely that viability of virus in air-borne particles is very important.

Infection might, however, be transmitted better in winter because of change in social habits. It is hard to avoid the conclusion that certain virus infections cause trouble only in newly-assembled closed communities just because of close and repeated contact between susceptibles in those units — in other words because of a social change. How far can differences in social behaviour between summer and winter determine the issue in respiratory infections generally? I am inclined to doubt their importance. There is very close crowding of people in towns all the year round. True, means of relaxation bring them more into the open air in summer than in winter, but differences of this nature only affect people for a relatively small part of their waking lives.

CHANGES IN VIRUS VIRULENCE

This, for most respiratory infections, seems the factor least likely to play a part. Experimental evidence suggesting a seasonal change in virus virulence is quite lacking. The matter is, however, worth considering in the case of influenza. The whereabouts of the virus between outbreaks is still obscure, though certainly sporadic cases may occur at any time. If inter-epidemic influenza virus is relatively avirulent, it may, when things become more favourable for it, have to build up its virulence by a number of person-to-person passages before attaining real epidemic strength. Such a conception could explain why, though colds break out in early autumn, the onslaught of epidemic influenza is so commonly delayed until the New Year.

CHANGES IN RESISTANCE OF THE HOST

We must now consider the possibility that cold viruses and others similar to it, do *not* vary in virulence and that they have adequate opportunity for person-to-person spread all round the calender and from the Poles to the equator. An effect of season or climate must then operate by raising or lowering resistance to infection to a point above or below the threshold of clinical disease. In the naval training station at Great Lakes, Illinois it was found that adenoviruses spread amongst recruits equally readily in summer and in winter, but whereas in winter clinical disease was common — 47.8 per cent had fever — in summer it was not much more than half that: fever occurred in 25.9 per cent. There were no differences with regard to conditions of crowding. Against this it must be recorded that volunteers inoculated with rhinoviruses at Salisbury show approximately the same incidence of disease, summer and winter. If resistance were higher in summer, the fact should reveal itself. I do not, however, want to lay too much emphasis on our Salisbury results. In the first place, when we inoculate the volunteers with intranasal drops, we must normally introduce a colossal number of virus particles, enough to blur differences due to the subtle factors we are considering. Further, the volunteers are not a random group: in winter, particularly, many intended to be used in a trial, either withdraw or are excluded because of spontaneous colds. We carry on studies on those who remain. We know that rhinoviruses may be recovered at times from noses of healthy people — that, in fact, there exist carriers. We know too, that at the time of an influenza epidemic, there are many subclinical as well as clinical infections, and moreover that the percentage of subclinical infections may vary. We have to think what could determine the difference between being a cold sufferer and a cold carrier, between a happy subclinical influenza case and a bed-ridden misery. Raising the body temperature activates a herpetic infection in some people who carry Herpes simplex virus in their noses. Could chilling have a comparable effect in cold-carriers? We need to know more about the possible effects of changes in the physiology of the nose in relation to immunity. The nose comprises a built-in mechanism for, amongst other things, ensuring a homeostatic control of the air reaching the lungs. Chilling the body surface causes changes in blood supply to the nasal mucosa and there is variable delay in the return of this to normal. Currents of air cause local desiccation of the mucosal surface, with interruptions in the normal continuous flow of a sheet of mucus. One can readily conceive that sudden changes in environmental conditions might upset the normal mechanisms of control, at least long enough to give a waiting virus its opportunity.

Latency of virus infections in now thought to be a normal every-day state of affairs. It has been shown that a number of viruses in tissue culture will infect and kill off many or most of the exposed cells. Yet some may remain and these may establish an equilibrium with the virus, such that the virus persists indefinitely and may or may not be regularly shed into the surrounding fluid, while the cells grow and appear to be unaffected. Adjusting the conditions of culture can lead to cure of cells from their infection, to the destruction of the cells or continuation of the state of equilibrium (Glasgow and Habel, 1962). In several instances it has been shown that the control of the virus is mediated by the action of interferon. This protein is produced by cells through contact with virus nucleoprotein, probably also other foreign nucleoproteins. It so alters the cell's metabolism as to halt virus replication and apparently acts as an anti-viral defence mechanism coming into operation before specific antibody can be produced. It appears that in chronically infected cells a balance is set up, just so much virus and so much interferon being produced that neither cell nor virus gains the upper hand. What happens in tissue culture is likely to occur also in the infected animal. There is some evidence suggesting that interferon production is not so good at lower temperatures. Whether temperature fall or something else is the operative factor, it is clear that there are many possibilities for so varying the conditions that a delicate cell–virus balance is upset. Several things might follow. The virus-carrier might himself be resistant to development of disease, but a tilting of the balance might cause him to shed more virus into his environment and so set up infection in others; or his latent infection might become an active clinical one; or the meteorological change might make another person more susceptible to the virus which the carrier was shedding.

All this makes a plausible theory as regards colds, but I can not quite see how it fits the story of Asian influenza in 1957. This hit North America and Europe at a time, in summer, when people's resistance was presumably good, so that largely subclinical infections could on the hypothesis just discussed have resulted. Why, then, did they not acquire specific immunity? Why did they go down in shoals in the autumn?

An encouraging feature of recent laboratory studies on colds is that a technique is now at hand for answering some of the questions I have propounded. One could discover, using isolated volunteers, whether rhinoviruses and other agents do spread from one subject to another better in winter than in summer; and whether, when they do spread, they produce symptoms equally well at any time of year. Russian workers have found that attenuated influenza strains, used as vaccines, can be made to infect the nasal mucosa more frequently in winter months.

There may be a unifying principle to be discovered or the answer may be a complex one, not necessarily the same for all pathogenic agents.

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THE ASSOCIATION OF CERTAIN METEOROLOGICAL VARIABLES WITH THE INCIDENCE OF RESPIRATORY DISEASE IN AN INDUSTRIAL CITY

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Abstract — The seasonal increase in the incidence of acute respiratory diseases which occurs every winter in the United Kingdom, especially in industrial communities, can be demonstrated by the trends in weekly numbers of claims to sickness benefits. Some results are given of a preliminary investigation into the possible associations of temperature, absolute and relative humidity with claims to sickness benefits, using weekly data collected over the last four winters for the city of Birmingham. Examination of the distribution of each meteorological variable over the 7 weeks prior to the increase in morbidity for the 4 winters failed to disclose any differences which would account for the gross differences in the subsequent morbidity patterns. However, over each complete winter (22 weeks) except for the first (1959–60), temperature and morbidity were negatively associated; and a barely significant negative association between absolute humidity and morbidity was found for the 1960–61 and 1962–63 winters. On pairing the value of the meteorological variable for a given week with the morbidity value for the following week, the significance of these associations was increased. No relationship between relative humidity and morbidity was detected.

Zusammenfassung — Der jahreszeitliche Anstieg der Morbidität an akuter Erkrankung der Atemwege, die in jedem Winter, besonders in den Industriegebieten in England, auftritt, lässt sich an den wöchentlichen Krankmeldungen zur Bewilligung von Krankheitsgeldern nachweisen. Einige Ergebnisse von vorläufigen Untersuchungen über eine mögliche Beziehung zwischen Temperatur, abs. und rel. Feuchtigkeit (R.F.) der Luft und Krankmeldungen für Birmingham werden berichtet. Die Korrelation der Verteilung dieser meteorologischen Faktoren während 7 Wochen vor dem Anstieg der Morbidität in 4 aufeinanderfolgenden Wintern ergab keine Beziehung. Wenn die Temperatur von 22 Wochen des gesamten Winters mit der Morbidität verglichen wurde, ergab sich für 3 Winter eine negative Korrelation, nicht dagegen im Winter 1959–60. Eine annähernd signifikante negative Korrelation zwischen absoluten Wasserdampfgehalt der Luft und Morbidität wurde für die Winter 1960–61 und 1962–63 gefunden. Beim Vergleich der gegebenen Parameter einer gegebenen Woche mit der Morbidität in der folgenden Woche wurde die Beziehungen strenger. Eine Beziehung zwischen R.F. und Morbidität lag nicht vor.

Résumé — En se basant sur les sommes hebdomadaires d'avis de maladie donnant droit à des indemnités, il est possible de démontrer l'augmentation saisonnière des cas d'affections aigües des voies respiratoires. Cette augmentation apparaît chaque hiver en Angleterre, surtout dans les districts industriels. On rapporte ici quelques résultats d'études préliminaires faites sur les relations possibles existant entre la température, l'humidité absolue et relative d'une part, le nombre d'avis de maladie à Birmingham d'autre part. La corrélation de la répartition de ces éléments météorologiques durant les 7 semaines précédant l'augmentation des dites affections n'a donné aucun résultat pour 4 hivers consécutifs. En comparant la température de 22 semaines de l'hiver entier avec la courbe du nombre des affections, on a obtenu une corrélation négative pour 3 hivers, mais pas pour celui de 1959 à 1960. On a trouvé une corrélation négative quasi significative entre la pression de vapeur absolue et le nombre de cas durant les hivers 1960 à 1961 et 1962 à 1963. En comparant le dit paramètre d'une certaine semaine avec le nombre de cas de la semaine suivante, la corrélation devient plus étroite encore. On n'a par contre trouvé aucune relation entre l'humidité relative et le nombre d'affections aigües des voies respiratoires.

THE seasonal increase in the incidence of acute respiratory diseases, which takes place every winter in industrial communities in the United Kingdom can be demonstrated by the trends in the numbers of: attendances at general practitioners' surgeries, new claims to sickness benefits under the National Health Service, and emergency admissions to hospital. The pattern of epidemics, as represented by these indices, differs from winter to winter and the weather is likely to be an important factor in determining the onset and course of these winter epidemics.

Over the last four years, the following data have been obtained for the city of Birmingham (pop. 1,115,000): (i) the daily number of patients with respiratory diseases admitted to hospital through the Birmingham Bed Bureau has been obtained. The Bed Bureau directs patients to all acute hospitals in the city and although not all emergency admissions take place through the Bureau the extent to which the Bureau is used certainly reflects the overall demand for admission: (ii) the number of new sickness insurance claims at each of the Ministry of National Insurance offices in Birmingham each week, so that it is possible to obtain the weekly numbers of claims for Birmingham as a whole. These refer to all illnesses of more than three days duration and to the working population only, but they do in fact reflect the trend for respiratory diseases alone.

We shall here be concerned with new sickness claims (total morbidity) although it is possible to show that there is a close correspondence between the distribution of total morbidity and hospital emergency admissions for three of the four winters.

The Birmingham Observatory publishes a weekly return giving for each day *inter alia:* the mean temperature, relative humidities at 6.00 hr, 12.00 hr and 18.00 hr, absolute humidity, rainfall and hours of sunshine each day. All the requisite data were available for the last four winters and in the graphs that follow appropriate scales have been chosen so that equal proportional changes of the two variables being compared are equally represented.

RESULTS

The first study that was made was for a possible relationship between the weekly number of sickness claims and mean weekly temperature (see Fig. 1).

The winter of 1959–60 was remarkable in view of the absence of any abnormally high morbidity values and this was true of the distribution of emergency respiratory admissions. In the following two winters there was a dramatic increase in incidence starting in the third week of December. As regards last winter, a pronounced peak occurred in the distribution of sickness claims during the first week of 1963, although the maximum value was much smaller than the peak values in the two previous winters, followed by fairly constant weekly values.

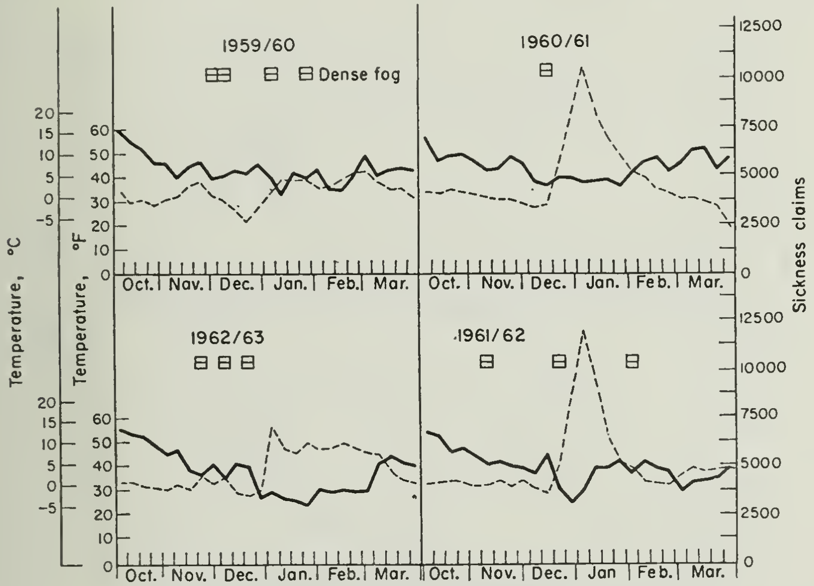

FIG. 1. Temperature variation and sickness claims

The results of virus studies carried out in Birmingham bear out these patterns. During the winter of 1959–60 there was no evidence of influenza in the community, except for a few dispersed cases of Influenza B. During the second winter Influenza A-2 was first isolated in the middle of December 1960. In the winter of 1961–62 Influenza B was isolated during the last week of 1961. There was no dominant virus in evidence during the 1962–63 winter. During the early part of the winter Influenza C was isolated and this virus was found again towards the end of February and during March. Influenza A was isolated during the last week of December 1962 and at the beginning of February and during the intervening four or five weeks there was evidence of Parainfluenza 3 in the community.

By examining the two graphs for the four winters one hopes to detect a pronounced difference in the pattern of temperature variation in the first winter from the second and third, and a similarity between the second and third in this respect. In fact in all three winters the mean weekly temperature gradually decreases during October and November and varies around 5° C during the first two weeks of the epidemic. The mean temperature over the seven-week period prior to the first week of increase in morbidity was the same for each of these periods (6° C) and the variation from week to week was similar in each winter.

Over the whole winter periods, the contours of the temperature graphs for the first two winters are similar with a striking difference in the morbidity curves; and there is a remarkable similarity between the morbidity curves for the second

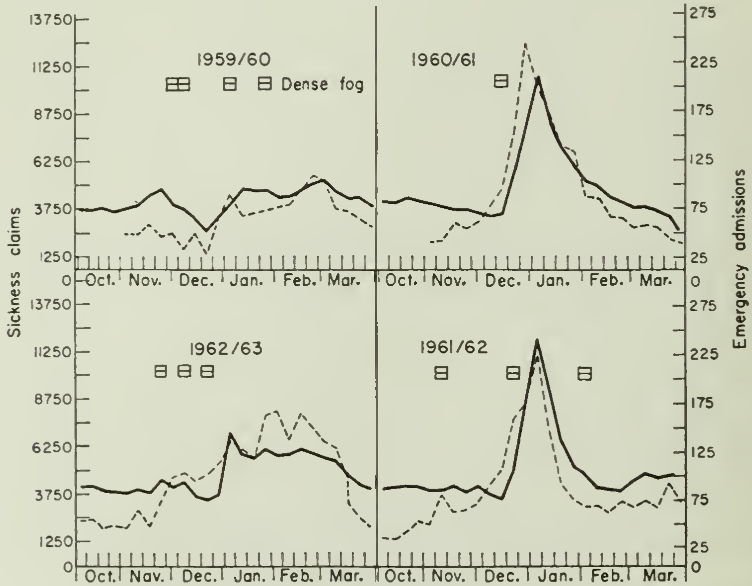

Fig. 2. Comparison of weekly bed bureau respiratory cases with National Insurance Claims

and third winter with dramatic difference in the temperature graphs — in the third winter there is a pronounced fall in temperature corresponding to the peak of the distribution of sickness claims.

The fourth winter was unusual in two respects: (i) the mean weekly temperature was below freezing point for ten weeks, and (ii) the first week of December 1962 was notable for an abnormally high level of air pollution. The mean temperature over the 7-week period prior to the increase in morbidity was 5° C and the fall in temperature at the end of December was followed by the increase in morbidity. During the 10-week period of relatively very low temperatures, morbidity remained fairly constant and no abnormally high values were recorded.

It is interesting that the distribution of weekly emergency respiratory admissions to hospital for this winter is different (see Fig. 2) in that there were four peaks superimposed upon an increasing trend and the cumulative Bed Bureau demand was greater than in any of the other winters. These admissions were mainly elderly patients with cardiac respiratory failure living in poorly heated conditions and were probably a direct result of the low temperature.

We next consider the weekly variation of absolute humidity in relation to the variation in weekly claims to sickness benefit. As humidity is correlated with temperature there is a rough similarity between the graphs on the next chart (Fig. 3)

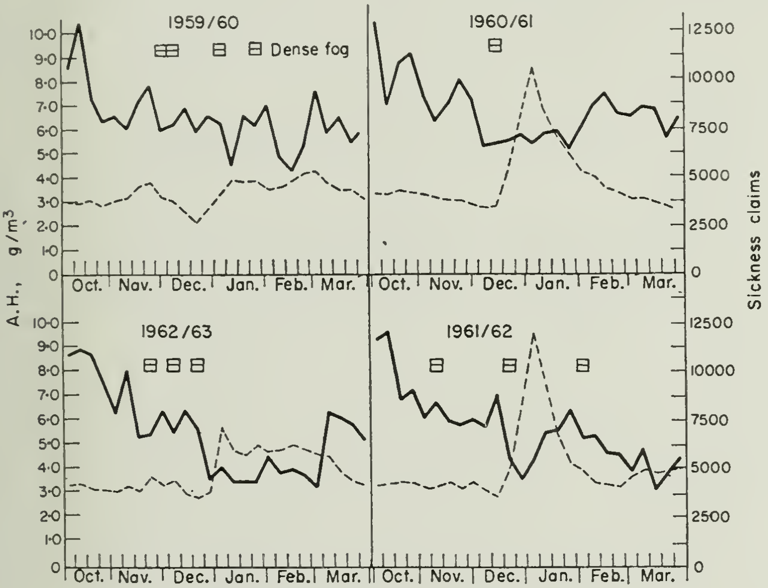

FIG. 3. Variation in absolute humidity and sickness claims

and the temperature graphs. Again the scales have been chosen to show equal proportional changes of the two variables by equal increments.

Comparing the second and third winters, for which the morbidity curves are similar, there is no similarity between the humidity graphs. The variation in humidity from week to week over the 7-week period prior to the morbidity increase is more pronounced in the second winter than the third. In the third winter the absolute humidity drops from about 7.0 to 4.0 g/m^3 at the same time as the morbidity curve increases. As regards the fourth winter the humidity varied around 6.0 g/m^3 prior to the increase in morbidity; it then fell to about 3.5 g/m^3 where it remained while the very cold weather persisted.

The weekly values of mean relative humidity (at 12.00 hr) have been plotted against the distribution of sickness claims on the next figure (Fig. 4). On this chart a scale which magnifies the variation in relative humidity to a greater extent than that of the weekly sickness claims has been used for illustrative purposes since relative humidity does not vary greatly from week to week.

Comparison of the picture disclosed for the four winters shows that there is some tendency for morbidity graphs to increase as the relative humidity increases but it is difficult either from these graphs or from the figures themselves to detect any association between the two factors. During the 7-week period prior to the morbi-

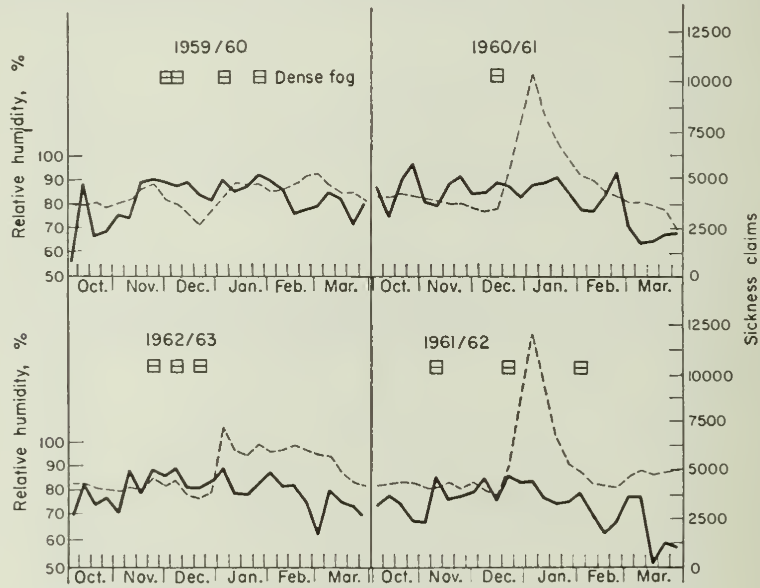

FIG. 4. Variation in relative humidity (noon) and sickness claims

dity increase the mean relative humidities in the first, second and fourth winters were the same (85 per cent); the mean for the third was less (80 per cent). The weekly variation was the same in the first, second, and fourth winters and less in the third.

DISCUSSION

This preliminary investigation of the possible associations of morbidity with three meteorological variables can only permit one to conjecture about the part that weather conditions play in determining the level of respiratory disease. The week has been taken as the unit of time because the epidemics in the two middle winters here considered are so "explosive" that any averaging over monthly periods would hardly seem likely to throw any light upon any possible circumstances prevailing which would trigger off such a rapid spread of infection. It may well be that it is these very short-term variations which may be propitious to the start of an epidemic.

Examination of the weekly results for these four winters failed to disclose any differences in the meteorological variables during the 7 weeks prior to increases in morbidity which would account for the gross differences in the subsequent morbidity patterns. However a simple correlation analysis over each complete winter between morbidity and meteorological variables gave the following results:

(1) There was a significant negative correlation between temperature and morbidity in each winter except the first, and in the last winter a very high level of significance was obtained.

(2) In the second and fourth winters a barely significant negative correlation between absolute humidity and morbidity was found, and in the first winter a *positive* correlation, barely significant statistically, between relative humidity and temperature was obtained.

When the value of each meteorological variable in turn for a given week was paired with the morbidity value for the following week the significance of the correlations obtained over the last three winters were considerably increased. None of the three meteorological factors were then found to be associated with morbidity during the first winter (1959–60). During this winter there was no evidence of influenza in the community, so that there was relatively little variation in the weekly sickness claims. Even though highly significant negative associations were found between morbidity and temperature and between morbidity and absolute humidity for the winter of 1962–63, there was no influenza epidemic on the scale of the two previous winters, and during the whole period of very low temperatures and humidity values there was not one single week in which an abnormally high level of morbidity was experienced.

This preliminary investigation has underlined the complex nature of the possible effects of weather conditions upon winter epidemics. In the United Kingdom, general practitioner records provide the most satisfactory source of data depicting the level of respiratory disease, and the College of General Practitioners has organized a survey whereby 70 doctors kept records throughout the last winter of all episodes of respiratory disease which they treated. The actual day of onset of illness was recorded and although the main purpose of this enquiry was to establish the effect of air pollution upon respiratory disease it should be possible to examine the daily or weekly incidence of disease in relation to these meteorological variables here considered; and to consider the possibility that it is not the actual daily or weekly values of temperature and/or humidity which are most closely associated with incidence, but the changes from day to day or from week to week.

THE ROLE OF AIR IN THE TRANSMISSION OF DISEASE

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Abstract – The role of air in the transmission of disease has been inadequately studied. This is true of its roles as an environment of microorganisms, vectors, and receiving hosts, and as a vehicle for the transmission of microorganisms. The processing of indoor air has been governed too much by considerations of human comfort and insufficiently studied for its pertinence in the promotion and maintainence of health, and the reduction of disease transmission. The fragmentary information available indicates that further studies would be of great interest and would probably improve our ability to control the spread of some infections. This appears to be particularly true for the study of the effects of levels of and variations in atmospheric moisture.

Zusammenfassung – Die Rolle der Luft bei der Übertragung von Krankheiten ist nur unvollkommen erforscht worden. Sie dient als Umwelt von Mikroorganismen, Vektoren und Wirtsorganismen und als Mittel für die Übertragung von Mikroorganismen. Die Wirkung der Raumluft ist für die Betrachtung der Behaglichkeitsverhältnisse des Menschen sehr betont worden, aber sie wurde nur ungenügend auf ihre Bedeutung für das Zustandekommen und die Aufrechterhaltung der menschlichen Gesundheit und für die Möglichkeit einer Verringerung der Krankheitsübertragung erforscht. Die nur unvollkommenen zur Verfügung stehenden Untersuchungen bedeuten, daß weitere Forschungen von großem Interesse wären und wahrscheinlich unsere Möglichkeit verbessern würden, die Ausbreitung einiger Infektionen zu kontrollieren. Dies scheint besonders wichtig zu sein bei der Untersuchung der Auswirkung der Größe und Veränderungen der atmosphärischen Feuchtigkeit.

Résumé – De rôle de l'air dans le transport des maladies a été, jusqu'ici, étudié de façon inappropriée. C'est surtout le cas dans son rôle de milieu ambiant des organismes microbiens, des agents vecteurs et des hôtes ainsi que comme véhicule des microbes. Le conditionnement de l'air à l'intérieur des locaux à trop été établi du point de vue du confort des habitants et pas suffisamment étudié pour son importance dans le maintient et l'amélioration de la santé humaine aussi bien que comme moyen de diminuer la propagation des maladies. Les renseignements disponibles, fort lacunaires il est vrai, indiquent que des recherches nouvelles seraient hautement souhaitables et amélioreraient vraisemblablement nos possibilités de maîtriser quelques épidémies. Ceci semble surtout important dans l'étude du niveau et des variations de l'humidité de l'air.

INTRODUCTION

In considering the role of air in the transmission of disease it is first important for us to recognize that the air forms part of the environment for everything on the earth. It is capable of serving as a vehicle for various contaminants. In disease transmission we are not only concerned with the character and behavior of the air, but with certain contaminants which it contains. Of particular interest are microorganisms, especially pathogenic ones, which originate from infected individuals and soil and decaying organic matter. There are apparently a number of spore-forming organisms which are able under certain circumstances to grow as parasites in animals, e.g. *Histoplasma capsulatum* and *Coccidioides imitis.* Other air contaminants of different types, such as pollens, dusts, smokes, fumes and gases, find their way into both indoor and outdoor air from various sources in nature and the activities of man.

In this paper we wish to consider the role of air: (1) as an environment of disease organisms, of vectors of such organisms, and of the receiving host of these parasites; (2) as a vehicle capable of transporting various contaminants from place to place with varying effectiveness; (3) as a fluid subject to processing by both natural and artificial forces, which are capable of rendering the air completely uninhabitable, or of improving it for animal habitation.

AIR AS ENVIRONMENT

Although air consists mainly of nitrogen and oxygen, much of the interest in air as an environment centers about a number of substances which are present in smaller and more variable amounts and in some of its physical properties. At present there is great interest in complex contaminations such as smog. The effects of smog on living things are frequently dramatic and devastating and probably also subtle as well. Whether or not contaminants of this type affect microorganisms or alter the susceptibility of animals to infection is not yet known.

MICROORGANISMS

Air contains no nutritive elements for microorganisms. It must be, therefore, a transitional environment in which they survive more or less well. With the exception of skin bacteria and spores, most microorganisms enter the environment in a moist state. They frequently come from a warm environment also. The most important characteristics of the air which relate to their survival appear to be temperature, moisture, and ultraviolet radiation. They are particularly sensitive to the latter, with the possible exception of spores which have not been well studied in this respect. Low temperatures are in general more favorable for survival than high, since they reduce the metabolic rate which allows longer viability in the absence of food, and also lower the rate of loss of moisture by reducing the saturation vapor pressure of the air. Most organisms are quite sensitive to high temperatures. The effect of moisture is variable and is in some instances closely related to temperature. Many bacteria and viruses are quickly killed by drying, whereas others will survive better in dry environments. For example, it has been known for many years that smallpox and vaccinia viruses can be kept for long periods in the dry state, but die quite rapidly when wet unless they are refrigerated. The seasonal fluctuation of smallpox apparently depends on this characteristic since it is most frequent when the vapor pressure is lowest (Rogers, 1948). It may seem strange to emphasize the importance of moisture in the survival of microorganisms, since all, or nearly all of them are now commonly stored in the lyophylized or dry state. This process is, however, a complex and artificial one. The relationship between lyophylization and normal survival in air is discussed in the very interesting chamber experiments of Dunklin and Puck (1948) and of Lester (1948). This work merits close study by anyone interested in the problem of survival of microorganisms in air and dust. The indications of great sensitivity of these organisms to unfavorable influences at relative humidities near 50 per cent appear to offer possibilities for the development of control measures. Recently Hemmes *et al.* (1960) have conducted additional chamber experiments of a similar nature which reinforce the earlier conclusions that humidity is a critical factor in the survival of microorganisms in air. Also new epidemiologic studies by Kingdon (1960) on influenza contribute further support for this point of view.

VECTORS

Many parasitic organisms are transmitted indirectly by arthropod vectors. The relations of the distribution, breeding, survival, and behavior of these vectors to meteorological phenomena are well known and adequately documented. Less obvious and less carefully studied is the effect of atmospheric variables on the microorganism in the vector. Bates and Roca-Garcia showed (1946) that the infection rate and development time of yellow-fever virus in Haemogoggus mosquitoes were affected by temperature, both in general being enhanced by higher temperatures with suitable fluctuation. They made no studies of the effect of humidity. Basu and Rao found (1939) that both high temperature and high humidity were needed for full development of filaria larvae in Culex mosquitoes; when either temperature or humidity was reduced the larvae, though present, failed to mature and the mosquitoes remained non-infectious.

ANIMAL HOSTS

Similarly to arthropod vectors, the effects of meteorological variables and air contaminants on man and other animals have been studied extensively (Sargent and Stone, 1954; Russel, 1957). The majority of these investigations have explored physiologic tolerance of, and adaptation to, extremes of variation. Some work has also been done within more normal limits of change. None of the information so derived appears to bear directly on the topic under consideration. The known reactions to changes in the atmosphere seem more likely to affect the course of established disease, rather than to influence the reception of infection.

With the exception of wounds, it is apparent that the principal receptor surfaces exposed to air are the conjunctivae, the mouth and throat, and the respiratory tract. We are not aware of any studies which have demonstrated effects of atmospheric variables on these surfaces as receptors of infection, although several suggestive physiologic observations have been made (Hill and Muecke, 1913; Mudd, Goldman and Grant, 1921; Andrewes, 1950; Stanhill, Cripps and Dickson, 1955).

It is commonly thought that natural resistance or susceptibility to infection (other than that due to presence or absence of antibody) depends on complex characteristics, rather than on a single trait. One should remember the famous experiments of Louis Pasteur (Vallery-Radot, 1926) in which he showed that the normally resistant hen could be infected with anthrax by lowering its body temperature a few degrees. Here resistance apparently depended on a single factor, unless one wishes to add the proverbial irritation of wet hens. Perhaps, the experiment should be repeated with an additional tranquilized control. At any rate it seems possible that simple meteorological alterations of modest magnitude could well affect susceptibility or resistance to infection with microorganisms.

AIR AS A VEHICLE

The vehicular role of air begins with contamination. This may be due to the suspension of dusts by air turbulence or by human and animal activities. Such dusts may contain microorganisms, which are usually but not necessarily attached to other material. Other sources of contamination are the animal respiratory tract and mouth which are constantly expelling droplets into the surrounding atmosphere. Many of these droplets contain living microorganisms. The larger droplets travel for a few feet at most and then settle out rapidly where they dry and leave dust residues. If a receptor person or animal is nearby, these droplets may be inhaled directly and establish transfer of infection. This direct droplet transfer is sometimes spoken of as a form of contact transmission, rather than as air transmission. The more numerous smaller droplets which are expelled evaporate within a small fraction of a second and leave droplet nuclei, sometimes containing microorganisms, which are so small that they remain suspended in the air for many hours (Wilson and Miles, 1955).

Once the vehicular function of the air is activated one must consider the interaction of several different effects: (1) the effect of air as an environment which we have already discussed; (2) dilution of the contamination by diffusion; (3) transportation by means of air currents and winds; (4) deposition in terms of fallout and impaction.

Although outdoor air forms an efficient vehicle for some plant diseases, such as wheat stem rust which can be spread over considerable distances, it has rarely been shown to be a vehicle for animal infections. In those cases where it is known to occur the transmission is associated with dust, and has been limited to short distances with the possible exception of violent storms (Manos, 1958). The only non-spore-forming organism known to be transmitted by outdoor dusts is the rickettsia of Q fever. This organism is thrown into the air by the movements of infected animals and appears to infect people who are, at the most, a few blocks distant (Beck *et al.*, 1949). Recent investigations of foci of histoplasmosis indicate a similar pattern, but further investigation is needed here. This may be due to dilution, to ultraviolet inactivation, to rapid fallout of organisms attached to rather large particles, or to some combination of these.

Indoor transmission of animal pathogens through the air is, on the other hand, a common phenomenon, especially in respiratory infections. Within buildings there are generally more sources of air contamination in the form of infected individuals in a given space than will occur outdoors. The burden of contamination in the air is therefore apt to be much greater. The dilution process is much less efficient indoors. Fallout is apt to be greater due to lesser degrees of turbulence. The lack of the scouring and suspending action of wind is more than made up for by a multitude of dust raising activities. All of these phenomena are enhanced as one moves farther from the equator; more people and animals are confined for longer periods to smaller and more tightly sealed quarters. While some of these problems may be alleviated by artificial ventilation, this can increase the spread of infection rather than reduce it if improperly carried out. The relative importance of these several factors in any given disease must be determined, and may vary under different circumstances as well as with different organisms. Desirable information here would be quantitative data on dosage of microorganisms to the air, their fate under various conditions and changes, and the effects of different quantities on the receiving host. Data of this kind are available for toxic substances in the field of industrial hygiene, and have proven very useful.

PROCESSING OF AIR

Among the types of processing to which air is subject are heating and cooling, wetting and drying, irradiation and filtration. All of these occur naturally and all can be carried out selectively by artificial means as well. Outdoor air is subject to continuous fluctuations of considerable magnitude in all of the above categories during the day–night alternation. In the larger scale alterations represented by the generation and modification of air masses extreme fluctuations are encountered. Contaminants in the air are necessarily exposed to extremes of irradiation, moistening, drying, and temperature. Decontamination is quite complete. However, it may be that time is the most important purifying agency affecting microorganisms in the air streams.

In the process of forming clouds and rain, particulate air contaminants tend to migrate to small growing droplets. Some of these droplets enlarge sufficiently to fall as rain, and in their falling collect and wash out additional contaminants. Other droplets evaporate leaving nuclei for later condensation and cloud or rain formation. Thus contaminants are frequently subject to extreme alternations of wetting and drying prior to eventual removal from the atmosphere.

Indoor processing of air is limited usually to temperature alterations conducive to human comfort. Thus the air in buildings is prevented in so far as is practical from undergoing the temperature alterations to which outdoor air is subject. Air motion is also kept at a low level since rapid air flow produces discomfort. Awareness of change in humidity of the air in man is much less acute than sensitivity to motion and temperature. Only extremes are annoying. Therefore, there is much less attention given to this aspect of air processing. There seems to be a generally accepted concept that comfortable animals are healthy animals, and that moderate unvarying temperature is the key to comfort. It appears to be quite comfortable for many pathogenic microorganisms too. Simpson has recently reviewed this problem (Simpson, 1958), illustrating the changes produced by winter heating and questioning the desirability of producing warmth accompanied by very low humidity. Study of the health aspects, as distinct from the comfort aspects, of optimal levels and variations in temperature and humidity has been very limited.

Filtration and washing of indoor air is used mainly in large buildings, principally for the removal of larger particles and odors. These processes depend on inertia of particles for their effectiveness, and hence are relatively inefficient for the removal of very small particles such as microorganisms. Electrostatic or thermal precipitation are more efficient for removing particles of smaller size, but their effect on microorganisms has not been extensively studied. Procedures for the suppression of dusts in order to limit the spread of infection have been a rather frequent subject of experiment. The conflicting results of these studies have recently been reviewed by Cruickshank (1957).

In recent years a number of experiments in the processing of indoor air with ultraviolet light have been carried out, particularly in schools (Cruickshank *et al.*, 1954). Perhaps the most important results of these studies has been to demonstrate that air transmission is an important factor in some diseases and not in others. In addition they have shown that diseases which are airborne indoors are also transmitted by other more intimate means, i.e. air transmission is not their only means of spread. In spite of the expense and work involved such processing has been felt to be worth while in selected circumstances. It should be pointed out that these experiments (and similarly directed ones with glycol and other vapors) have been very limited up to the present time. Another form of radiation, that of visible light is commonly applied to hens to increase egg laying. While it may seem that this could have little bearing on the problem under discussion, gestation is known to increase the excretion of several disease organisms, and may in addition alter receptivity to infection.

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SEASONAL EFFECTS ON RESPIRATORY DISEASE IN RELATION TO SPECIFIC VIRUS INFECTIONS

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Abstract – Respiratory diseases are the commonest mode of illness and account for more morbidity annually than any other disease. The high frequency seems to be world wide. Moreover, waves of increased incidence are synchronous over vast geographical areas (synchronicity) and the actual incidence reaches a similar level in all places (isomorbidity). Most respiratory diseases show a close inverse association with the seasonal temperature. All these problems require explanation. It is important to determine which individual virus infections follow the general trend and which do not. Each virus must be studied individually and without preconception. This work has been begun and examples are given.

Zusammenfassung – Die Erkrankungen der Atemwege stellen die verbreitetste Art von Krankheiten dar und führen zu einer größeren jährlichen Sterblichkeit als irgend eine andere Erkrankung. Die große Häufigkeit scheint eine weltweite Tatsache zu sein. Zudem sind Wellen des Anwachsens der Erkrankungen synchron über weite Gebiete (Synchronität) festzustellen, und das akute Auftreten erreicht an allen Orten eine ähnliche Höhe (Isosterblichkeit). Die meisten Erkrankungen der Atemwege zeigen eine enge inverse Beziehung zur jahreszeitlichen Temperatur. Alle diese Fragen müssen erforscht werden. Es ist wichtig zu bestimmen, welche individuellen Virusinfektionen dem allgemeinen Trend folgen und welche nicht. Jedes Virus muß individuell und unvoreingenommen untersucht werden. Diese Arbeiten haben begonnen, es werden Beispiele hierfür gezeigt.

Résumé – Les affections des voies respiratoires sont les maladies les plus répandues et elles provoquent chaque année le plus de décès. Cette constatation semble valable dans le monde entier. En outre, ces maladies se déclarent en général brusquement dans de vastes régions (sychronisation). L'acuité des pointes en est en outre semblable en tous lieux. La plupart des affections des voies respiratoires présente une relation inverse très étroite avec la température. Toutes les questions que posent ces constatations devraient être étudiécs. Il est important de déterminer quelles maladies à virus suivent la tendance générale et lesquelles ne la suivent au contraire pas. Chaque virus doit être examiné pour lui-même et sans parti-pris. De telles études ont déjà été entreprises et on en donne quelques exemples.

INTRODUCTION

The respiratory group of diseases has a number of special peculiarities which distinguish it from any other group of illness. The peculiarities are those of frequency, synchronicity, isomorbidity and seasonal distribution.

Frequency

By far the commonest mode of being ill is to suffer a respiratory disease. In a volunteer study lasting 4 years, in which some 350 persons took part, the annual average per person was 7 such illnesses, each lasting an average of 10 days, i.e. 70 days of respiratory morbidity annually. (Simpson, 1958). Dingle and his colleagues in Cleveland found a similar morbidity amongst his volunteer group (Dingle *et al.* 1953). Sutton found a similar frequency in Trinidad (not yet published). The first problem is: Why is this group of diseases so common and apparently ubiquitous?

Synchronicity

Over vast areas as shown by van Loghěm (1928) and Frost and Gover (1932) morbidity rises and falls synchronously. What is the influence which is responsible for this remarkable behaviour?

Isomorbidity

In addition to the synchronicity of the waves and troughs of incidence, the attack rate itself is approximately equal at any given date over wide areas. (van Loghěm, 1920). This phenomenon also requires explanation.

Seasonal Swing

It has long been realized that respiratory diseases are more common in the winter, but it is only recently that it has become evident how closely associated is this group of diseases with the seasonal temperature. The results from the Cirencester volunteer group showed (Hope-Simpson, 1958) that for each rise of 1° F (0.56° C) in the seasonal temperature there was a fall of 1 per cent in the morbidity from respiratory disease, and conversely, as the temperature falls, the morbidity rises *pari passu*. Evidently, whatever the aetiology of colds and other respiratory diseases, there is some important influence, probably dependent on the seasonal temperature, which either inhibits or promotes the appearance of respiratory disease. It is clearly of the highest interest to identify this unknown seasonal agency and investigate its mode of action.

Methods of Study

In attempting to identify the influences at work on respiratory diseases one becomes aware that certain diseases follow the main seasonal pattern whilst others do not do so. Sore throats, for example, follow a quite different pattern with a tendency to a greater summer prevalence (Fig. 1 and Table 1). Influenza usually attacks in the winter but does not do so annually. When it strikes, it is so rapid and so widespread that it drags the morbidity curve violently away from its normal close association with a curve of seasonal temperature (Fig. 2). Evidently, much can be learned from a detailed study of the aetiology of those diseases which do and those which do not follow the seasonal pattern.

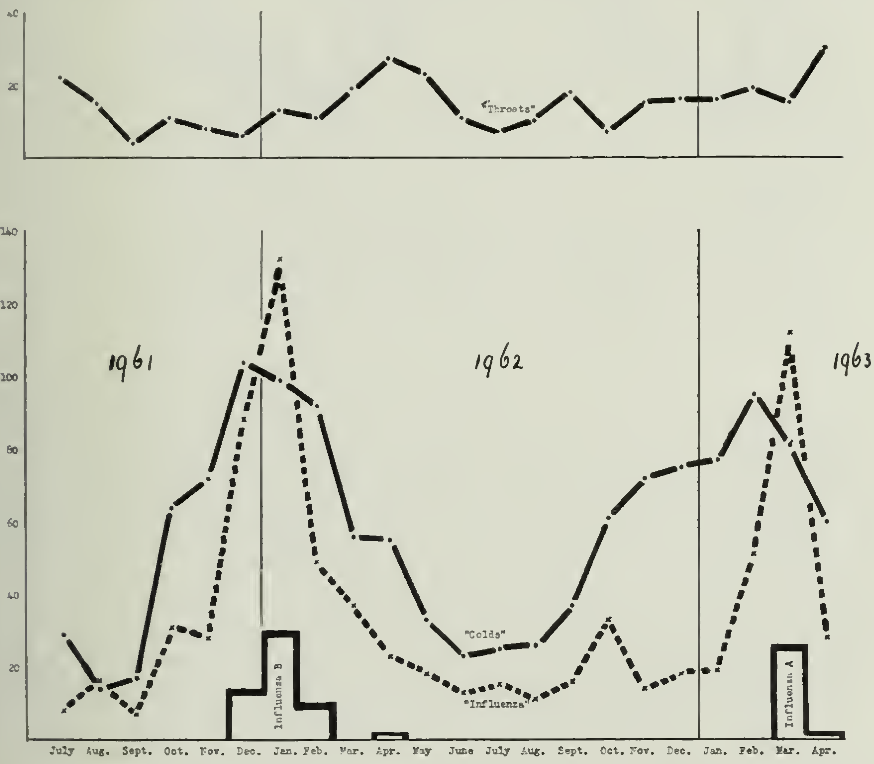

FIG. 1. Morbidity from clinical influenza, colds and sore throats in a general practice. It is clear that the sore throats do not follow the same seasonal pattern. The histograms show the isolation of influenza viruses coinciding with epidemics of clinical influenza

These respiratory diseases are usually considered to be caused by transmission of an infectious agent from case to case as in measles and probably also in influenza. This may be the case for many of them. Some of the group, on the other hand, may be caused by agents which are usually latent in the human body, but periodically disturbed into activity which is manifested as an illness. The classical model for such a latent agent is herpes simplex or malaria. Here again we are facing a problem of fundamental importance. Which of these respiratory diseases

Table 1. Prevalence of Different Types of Acute Respiratory Illness in a General Practice

Year	Month	Colds	Influenza	Throats
1961	July	29	8	22
	August	14	16	15
	September	17	7	4
	October	64	31	11
	November	72	28	8
	December	104	88	6
1962	January	99	132	13
	February	92	49	11
	March	56	37	19
	April	55	23	27
	May	33	18	23
	June	23	13	11
	July	25	15	7
	August	26	11	10
	September	37	16	18
	October	61	33	7
	November	72	14	15
	December	75	18	16
1963	January	77	19	16
	February	95	51	19
	March	81	112	15
	April	60	28	30

are due to direct case to case transmission, which are due to periodical reactivation of a latent agent, and which use both modes of behaviour?

From the foregoing discussion it appears that the seasonal influence may act in more than one way. Firstly, it may act on a latent organism, stimulating it to activity or inhibiting it. Secondly, it may act upon viruses which depend upon continuous transmission from case to case for survival, for example, by increasing or decreasing the efficiency with which they are transmitted. Thirdly, in the case of certain viruses the seasonal influence may act both upon a latent phase and upon a phase of transmissibility. The simple picture of seasonal temperature association may thus be found to depend upon a complicated aggregation of different sorts of dependence.

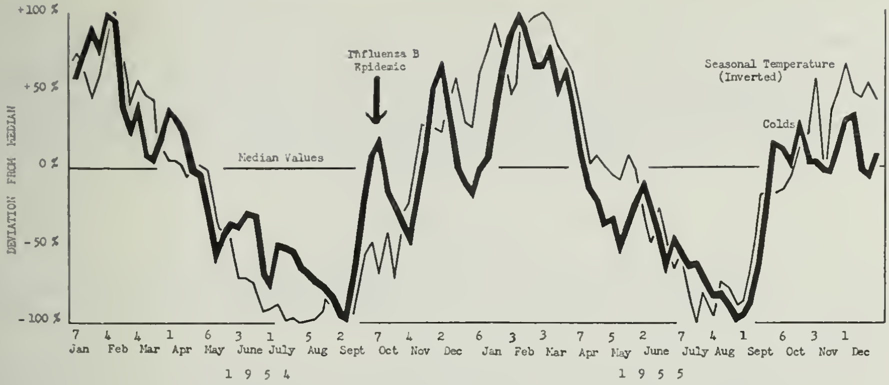

FIG. 2. The association between morbidity from respiratory disease (thick line) and the inversion of the seasonal temperature (thin line). Note how the influenza epidemic disturbs the relationship

(Modified from a figure in *Proc. Roy. Soc. Med.* 1958, **51**, 267.)

The Natural History of Individual Viruses

Information obtained about the natural history of a particular virus is sometimes used in theorizing about other viruses. This may be misleading. There is no *a priori* reason to suppose that the life history of one species of parasite is necessarily similar to that of another species, even a nearly-related one. The converse is more likely to be the case. Nearly-related species tend to occupy widely different ecological niches because they thereby avoid competition with one another. The commoner the parasite the more likely it is to have a different life history from its near relatives. Elucidation of the biology of, for instance, Myxovirus parainfluenzae type 1 will not necessarily cast light upon that of types 2 or 3. Each agent requires to be studied individually and without preconceptions.

The Epidemiological Research Unit at Cirencester has had a general practice of some 3500 persons under continuous epidemiological surveillance for 17 years. For the last two years a Public Health Laboratory Service virus laboratory installed in the premises by the Medical Research Council has been continuously sampling the respiratory diseases affecting this population. The research is still in its preliminary stages, but some results of interest have emerged.

An aetiological agent can at present be discovered only in some 20 per cent of cases. Not unexpectedly, the virus flora proves to be more important than the bacterial flora. Certain viruses – Influenza A and B, respiratory syncytial virus – appear in well-defined epidemics and disappear again. Others, e.g. Rhinovirus H, appear sporadically throughout the year. The parainfluenza viruses seem to occupy an intermediate position in this respect, sometimes presenting in epidemics, sometimes endemically.

One virus only, respiratory syncytial, shows a strong preference for a particular age group, 90 per cent of isolations being from children of 6 years of age or less. Clearly much work is needed to fit these agents into their proper setting in the overall seasonal epidemiological picture, and a challenge awaits us in the 80 per cent of respiratory diseases from which no agent can yet be isolated.

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SEASONAL VARIATIONS IN THE TRANSMISSION OF INFLUENZA VIRUS INFECTION IN MICE*

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Abstract – In an experimental model designed to study transmission of influenza virus infection in mice, significant seasonal variations in the rate of transmission have been observed. These variations can be explained in part by variations in relative humidity, since transmission was more frequent at low relative humidity than at high relative humidity. Variations in relative humidity alone do not adequately explain seasonal variations in transmission, since appreciable seasonal variations were observed when experiments were conducted in environmentally controlled quarters.

Zusammenfassung – In einem Versuch zum Studium der Übertragung der Infektion mit dem Influenza-Virus bei der Maus wurden überzufällige jahreszeitliche Schwankungen bei der Zahl der Übertragungen beobachtet. Diese Schwankungen können zum Teil durch Schwankungen der relativen Feuchte erklärt werden, weil die Übertragung häufiger bei niedriger als bei hoher relativer Feuchte erfolgte. Schwankungen der relativen Feuchte allein können die jahreszeitlichen Schwankungen bei der Übertragung nicht völlig erklären, weil deutlich jahreszeitliche Schwankungen beobachtet wurden bei Versuchen, die in Räumen mit kontrollierten Luftbedingungen durchgeführt wurden.

Résumé – Dans un essai d'infection de rhume sur des souris, on a pu observer une corrélation significative entre la contamination et la saison. Ces variations de la contamination peuvent en partie s'expliquer par les fluctuations de l'humidité relative de l'air. En effet, elle est plus fréquente par faible humidité relative que par humidité élevée. Cependant, les variations de l'humidité ne peuvent, à elles seules, expliquer les différences saisonnières de la contamination. En effet, on en a constaté de très nettes même dans des locaux dans lesquels cet élément météorologique était maintenu constant.

INTRODUCTION

In temperate areas of the world, influenza has tended to be most prevalent during winter months (Herrington and Moriyama, 1939) and to decline rapidly in incidence with the appearance of warmer weather (Zhadanov, 1959). A number

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of hypothetical explanations for the "winter factor" in influenza have been offered, including: crowding of people in poorly ventilated indoor environments (Jordan, 1960), activation of masked infections provoked by wintertime stresses (Shope, 1958), and the greater susceptibility of influenza virus to inactivation of airborne droplet nuclei at higher relative humidity (Harper, 1961). Considerable epidemiologic or experimental evidence has been gathered to support each of these views, but difficulty in defining all of these complicated factors in naturally occurring outbreaks makes it virtually impossible to assess the importance of each.

An experimental model has been developed and employed in our laboratory to study the transmission of influenza virus infection in mice (Schulman and Kilbourne, 1963). In the course of these experiments, observations were made with regard to seasonal variation and the effect of relative humidity. The influence of these factors on transmission of influenza virus infection in mice constitutes the basis of the present report.

MATERIALS AND METHODS

Mice

Male adult Swiss albino mice from two sources were used in all experiments. The age and breed of mice have been shown in previous studies to influence the frequency of transmitted infection (Schulman and Kilbourne, 1963), but no attempt will be made in the present report to distinguish these factors.

Virus

A strain of influenza A2 (Asian) virus adapted to mice by 27 consecutive intranasal inoculations was employed. In all experiments, the virus was derived from a common seed maintained at $-67°$ C until the time of the experiment. Ten-fold dilutions of this seed were made in pH 7.3 phosphate buffered saline (PBS) for use as nebulizer fluid.

Aerosol Procedure

Mice inside a modified autoclave chamber were exposed to an aerosol mist of influenza virus. The aerosol was generated by a Vaponephrin nebulizer under a pressure of 15 lb/cm^2. Under the conditions of the aerosol procedure, 0.3 cm^3/min of nebulizer fluid was introduced as a fine mist (95 per cent of the particles were less than 5 μ in diameter). A measured continuous vacuum was applied to the chamber so that 25 l of air/min flowed through the chamber. Five liters per minute entered through the nebulizer, and the remaining 20 l/min entered through a room air source at right angles to the nebulizer opening. Measurements of relative humidity and temperature inside the chamber were made at 5-min intervals with a *Hygrophil* apparatus. Mice were kept inside the chamber for 45 min and were exposed to an estimated 100 mouse infective doses of virus.

Contact Procedure

Previous studies had shown that infected mice transmitted influenza virus infection almost exclusively in the period from 24 to 48 hr after initiation of their infection (Schulman and Kilbourne, 1963). Consequently, in all experiments uninfected mice were exposed to the previously infected animals during this interval only. Exposure to transmitted infection was initiated in two different ways: in small stainless steel cages with two infected and two uninfected mice in each cage or in the large chamber, where 10 uninfected mice were exposed to 10 previously infected animals. When exposure to transmitted infection was initiated in the large chamber, air flow could be regulated and periodic determinations of relative humidity and temperature inside the chamber were made.

Demonstration and Titration of Pulmonary Virus

After a 24-hr period of exposure to transmitted infection, the previously uninfected animals were removed and quarantined in individual cages for 48 hr. Their lungs then were removed and ground in tubes with teflon grinders as 10 per cent suspensions. Ten-fold dilutions of each of these suspensions were inoculated into the allantoic sacs of chick embryos. After 48 hr of incubation allantoic fluids were harvested and examined for viral hemagglutinin in 1 : 4 dilution.

RESULTS

Seasonal Variation in the Incidence of Transmitted Infection

Table 1 summarizes four groups of experiments done over a 2-year period. The first two groups of experiments were carried out in rooms equipped only with ordinary room air conditioning and with steam and electrical heating. The last

Table 1. Seasonal Variations in the Frequency of Transmitted Influenza Virus Infection in Mice

Environmental controls	Season	Number of contact mice infected*
Room air conditioner and steam heat	July–October	1/120 (0.8%)
	December–January	48/216 (22.2%)
Year round controls 72° F 50% R.H.	May–October	109/320 (34.1%)
	November–April	192/320 (58.2%)

* Exposure to transmitted infection in small cages, two infected mice and two contact mice in each cage.

two groups of experiments were made in environmentally controlled animal quarters where a year round temperature of 72° F and 50% R.H. were maintained. In all the experiments the same strain of mouse-adapted influenza A2 virus, originating from a common seed kept at $-67°$ C was employed. Similarly, the method of aerosol infection and the duration and circumstances of the contact period were identical. However, the first two groups of experiments are not strictly comparable with the last two in that mice of differing ages and strains were employed.

The upper part of Table 1 demonstrates that in ordinary animal quarters without sensitive controls of temperature and humidity the frequency of transmitted infection was considerably greater during the winter months than during summer months. The lower part of Table 1 summarizes the results of experiments made at different times of the year in environmentally controlled animal rooms. Although seasonal differences in the rates of transmission were less striking when temperature and humidity were controlled, appreciable seasonal differences were observed.

Effect of Relative Humidity on the Incidence of Transmitted Infection

Ten previously uninfected mice were placed in a wire cage inside the aerosol chamber with 10 mice infected 24 hr earlier with influenza virus and a 24-hr period of contact permitted with food and water provided. Air flow through the chamber was controlled for each experiment at 1.4 l/min. Calcium chloride was placed in shallow pans inside the chamber to try to reduce relative humidity. Temperature and relative humidity inside the chamber were measured four times during the 24-hr period of contact. Forty-eight hours after the end of the contact period the previously uninfected mice were examined for transmitted infection by inoculating ground lung suspensions into chick embryos.

Table 2. Effect of Relative Humidity on the Frequency of Transmitted Influenza Virus Infection in Mice

Mean Relative Humidity*	Number of Contact Mice Infected⁺
greater than 50% (51–70%)†	13/30 (43.3%)
less than 50% (40–50%)‡	30/40 (75.0%)

* Mean of 4 determinations of R.H. during contact period.

⁺ Exposure to transmitted infection in a closed chamber: air flow 1.4 l/min.; 10 infected mice and 10 contact mice.

† Three experiments.

‡ Four experiments.

The results of 7 such experiments made within a 6-week period from 20 February to 1 April, are summarized in Table 2. The rate of transmission was significantly higher in those experiments where the mean relative humidity was less than 50 per cent than in those experiments where the relative humidity was greater than 50 per cent.

DISCUSSION

Previous experiments in this laboratory (Schulman and Kilbourne, 1962) demonstrated a decline in the rate of transmission of influenza virus infection in mice as relative humidity increased from 47 to 70 per cent. These observations were confirmed in the present studies conducted in an enclosed aerosol chamber where relative humidity could not be accurately controlled. In addition, the marked seasonal variation observed in experiments employing small open cages in animal rooms with inadequate environmental control also suggests that high relative humidity is unfavorable to transmission of influenza virus infection. Harper has shown (1961) that aerosolized influenza virus in contrast to polio virus survives less well at higher than at lower relative humidities. It is of interest, however, that when relative humidity was controlled, significant seasonal variations in transmitted infection were still present. These variations are not due to seasonal differences in the course of infection of artificially infected (infector) mice (Schulman and Kilbourne, 1963). Neither can these seasonal variations be explained by change in the virus, by differences in crowding or by stress due to exposure to cold since all the experiments were exactly alike in design, differing only in the season when they were conducted. It is, therefore, necessary to find other explanations for the seasonal variations observed in these experiments. It is possible that such explanations may also be applicable to the seasonal variations in human influenza.

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ÜBER DAS EPIDEMISCHE AUFTRETEN DER GRIPPE IM GEBIET DER PROVINZ POZNAŇ IN ABHÄNGIGKEIT VOM WITTERUNGSABLAUF

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Zusammenfassung — Es wurden auf Grund von synoptischen Daten von Polen in den Jahren 1955–1959 der den Grippeepidemien vorausgehende Witterungsablauf und die Wetterverhältnisse während der Epidemien untersucht. In dem 5-jährigen Zeitraum traten 4 Grippeepidemien auf und zwar zweimal im Jahre 1955 und je einmal in den Jahren 1957 und 1959 (3 Grippeepidemien im März und eine im November). Die Wetterlagen wurden in 2 Gruppen eingeteilt, eine umfasst Wettersituationen mit schwachen Luftdruckgradienten, zur zweiten Gruppe zählen wir alle übrigen Luftdrucklagen. Auf dieser Grundlage wurden Kurven des Grippeepidemieverlaufs (wöchentliche Erkrankungszahl) den gradientschwachen Drucklagen gegenübergestellt. Aus dieser Analyse geht hervor, dass 5–6 Wochen vor dem Ausbruch einer Grippeepidemie eine länger andauernde Zufuhr von warmen Luftmassen auftrat, der eine länger anhaltende Hochdruckwetterperiode folgte.

Das Ansteigen der Grippeerkrankungen erfolgt in der Endphase der Hochwetter und führt zu einer Massenerkrankung beim danach folgenden überwiegend zyklonalen Störungswetter. Das Erlöschen der Epidemie erfolgt beim wiederholten Eintreten der Hochdruckwetter. Ohne vorherige, länger andauernde und stark entwickelte Hochwetter wirkte das zyklonale Störungswetter jedoch nicht als "Grippewetter" (in Jahren ohne Grippeepidemien).

THE SIGNIFICANCE OF THE THERMOREGULATION MECHANISM FOR METEOROTROPIC INFECTIOUS RESPIRATORY DISEASES

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Various observations in the Netherlands are described which suggest that a decrease in the thermoregulation efficiency of the body may create a greater susceptibility to infectious agents. (1) The spontaneous development of common cold epidemics in different parts of the country during meteorological periods, which seriously affect the hypothalamic thermoregulation efficiency. (2) The yearly influenza peak in the Netherlands, around February, which may be related to the usually low humidity and wind-speed in this period, but which effect is probably accelerated by the decreased thermoregulation efficiency of the body as a result of the preceding colds months and the accompanying changes in the physico-chemical state of the blood such as γ-globulin level. (3) The decrease in infectious diseases of asthmatic patients after a simulated high altitude treatment in low pressure climatic chambers which seems to be related to an improvement of the thermoregulation efficiency.

CONCLUDING REMARKS

C. H. ANDREWES

DISCUSSION on colds and influenza was related to the methods of obtaining data of morbidity and mortality and the statistical problems involved; to the different results obtained according to whether one studied more serious illness involving absence from work or the minor illnesses not normally reported to a doctor; to the probably different effects of weather and climate on infections spreading from case to case and on latent infections activated by environmental change; to the curious difference in spread of influenza infection amongst mice in summer and winter (Schulman) even though environmental conditions were not very different.

Peaks in respiratory illness occurred in children when they returned to school in September each year both in Trinidad and England. The peak in incidence in England continued throughout the winter but was transitory in Trinidad.

In relation to temperature measurement used it is important to remember the unit of time. The use of the week or month mean temperature is very highly correlated with all other measures of temperature. In using day to day recording changes of temperature it must be remembered that day to day variations in illness are affected by other factors, e.g. holidays.

Various speakers had been using "average" temperatures in their studies. But biometeorological experience in Holland (Tromp) had shown this to be a dangerous procedure because periods with the same "average" temperature but different hourly amplitudes may have entirely different biological effects.

The possibility was considered by Tromp that a change in the permeability and blood-flow in the mucous membranes of the nose and lungs could affect the penetration of viruses and bacteria. If this were the case it would be an important factor because strong cooling or heating in the atmosphere affected the capillary resistance and permeability probably through a hypothalamic–pituitary–adrenal mechanism.

It was thought that influenza should be considered separately as the phenomenon of synchronicity does not apply. Undoubtedly there are differences in time between peaks in countries and in different parts of one country. Meteorological factors may play a part at the start of an epidemic but not after it has begun actively to spread.

The first increase in the year noted by various workers happens to occur at a time not only of meteorological change but also of cultural change. Families gather together to eat (or overeat), children are earlier home from day school or move from one community to another. Even among groups hospitalized for long-term conditions such as veterans in long-stay centres there are wide fluctuations in hospital admissions at this time of the year. The same type of cultural as opposed to meteorological effect of time of year could occur with the opening of school.

In the Pacific north-west of the United States, there appeared to be an increase in respiratory disease in early spring, which is not associated as much with such cultural changes. Such an observation emphasizes the desirability of having the WHO establish wide-spread monitoring of respiratory morbidity.

In regard to the possibility that chilling caused "colds" it was pointed out by Tromp that some people are abnormally sensitive to feelings of chill in the early stages of a cold. Their thermoregulation efficiency is not very efficient. The study of this aspect was suggested during future common cold research studies.

CO-OPERATION WITH WHO

The lack of knowledge about the incidence of respiratory infection in different countries was considered to be unfortunate and a resolution on this subject was drafted for transmission to WHO.

WHO expects to set up a survey team to investigate the prevalence of chronic diseases in various parts of the world. Observer bias would at least be partially avoided as the team would examine random samples of the population. It would be a simple matter to include questions on acute respiratory disease and such simple methods of examination as might be useful to determine its prevalence in different parts of the world.

International comparative studies are already in progress in cardiovascular and chronic respiratory disease. WHO helped in some of these by holding training sessions.

Many problems could be solved if better diagnostic reagents were available, e.g. serotypes of rhinoviruses. It may be that WHO could help here also. WHO is already aware of this need but the problem is difficult and will not be rapidly solved.

Although it would be desirable to include data on Rheumatism. Silicosis and other diseases, too much cannot be attempted at once.

In such a survey clinical records and virological data as far as possible must first be obtained. Various questions need to be considered including the following 3 basic questions:

(a) *The method of defining populations* – random samples identical in all possible respects or volunteers.

(b) *The information desired* – the same information on different groups over a period or on the same group; virus isolations or symptoms or disability. The social behaviour may be important and data on attendance at gatherings might be included.

(c) *The methods for obtaining the information* – the questions and methods of standardization are of great importance.

THE EFFECT OF IODINE AEROSOLS OF DIFFERENT AIR MASSES ON THE HEAT PRODUCTION OF MAMMALS

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According to previous investigations by the author there was a relationship between the iodine aerosol content in the air and the heat production in rats (L. Balogh and A. Palfy: Air iodine content and energy exchange of the rat. *Acta physiol. Hung.* **18**, 65, 1960). Heat production was high with a low iodine aerosol content and decreased with increasing iodine in the air up to 0.3 μg iodine/m^3 and increased again with a further increase of iodine concentration (0.5 $\mu g/m^3$). The author reported about the role of the thyroid in this relationship. It was found that with a higher content of medium sized iodine aerosols in the continental air masses there was a lower heat production and 132 I uptake while there was a higher heat production and radioiodine uptake with maritime air masses with a lower content of large sized iodine aerosols.

ATMOSPHERIC IONIZATION AT HEALTH RESORTS AND ITS ROLE IN BIOCLIMATOLOGY

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OBSERVATIONS at health resorts demonstrated that physiological shifts in the organism occurring in a number of cases under the influence of certain atmospheric conditions cannot be completely explained by the action of the ordinary meteorological factors. There is evidence that atmospheric ionization plays an important role in the vital activity and state of health of man and it is necessary to take into consideration this new factor in evaluating the climato-therapeutic advantages of health resorts. In a number of localities with similar geographical and climatic conditions there was an increased concentration of light atmospheric ions which correlated with the favourable effect of the climate on the state of health of patients with pulmonary tuberculosis, bronchial asthma, hypertension, joint diseases, vasomotor rhinitis and sinusitis and diseases of the peripheral nervous system. This was especially true in cases when negative ions were predominant. On the other hand it was observed that during specific weather conditions, in the presence of local winds (fan, North-West, etc.), the number of positive ions in the atmosphere increased considerably and this coincided with a deterioration in the condition of tuberculosis patients with disturbances of the nervous system and the appearance of dyspnoea and headaches.

PHYSIOLOGICAL AND CLINICAL OBSERVATIONS ON THE EFFECT OF IONIZED OXYGEN ON POLIOMYELITIS PATIENTS

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Fifty patients, aged 18–59, with poliomyelitis paralysis were treated either by inhalation or subcutaneous injection of ionized oxygen. Injection of positively ionized oxygen was painful and was followed by a fall of the skin temperature of 2 to 5° C, the minimum temperature being reached after 2 to 5 hr. Injection of negatively ionized air was painless and produced an increase of the skin temperature of 1 to 5° C 15 min after the injection. After 3 weeks treatment with negatively ionized air patients felt better and the limbs were definitely warmer and cyanosis had diminished. Similar results were seen when the positively or negatively ionized oxygen was inhaled instead of injected. The injection of negatively ionized air also led to an increase of the blood catalase, of the serum γ-globulins and an increase in the case of low and a decrease in the case of high corticosteroid excretion. There was also an increase in the strength of the muscles and serum cholinesterase activity. It is concluded that treatment with negatively ionized oxygen has a marked vaso-dilatatory action and a normalizing effect on adrenal cortex activity when given either by inhalation or injection and may be of therapeutic value in neurological and other diseases.

UNTERSUCHUNGEN ÜBER DIE BIOLOGISCHE WIRKUNG DER ELEKTRO-AEROSOLE UND DER DIREKTEN AUFLADUNGS-THERAPIE AUF DAS VEGETATIVE NERVENSYSTEM

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Die Beobachtung des Effektes der Luftelektrizität ist wegen des gleichzeitigen Einwirkens mehrerer klimatischer Faktoren meist schwierig. Bei der künstlichen Herstellung von statischen Ladungen sind die physikalischen Verhältnisse besser definiert und können variiert werden. Die ausgelösten Effekte und auch die biologische Wirkung sind daher leichter zu beurteilen. Dies gilt vor allem für die Anwendung in der Therapie. Im Rahmen eigener Untersuchungen von mehreren tausend Krankheitsfällen wie Asthma bronch., chron. Bronchitis, Herz- und Kreislaufstörungen, Allergien, rheumatischen Erkrankungen, Migräne, alle Formen der vegetativen Dystonien und Keuchhusten stellte ich fest, dass sowohl die negative als auch die positive Ladung günstige biologische Wirkung haben bei entsprechender Berücksichtigung der vegetativen Reaktionslage und des Reaktionsverlaufes. Die vegetative Reaktionslage wurde bestimmt durch Messung der Hautwiderstandswerte in den Haut-Segmenten des Menschen li. und re. von Kopf bis zum Fuss und der Reaktionsverlauf wurde während der Behandlung bei Einwirkung von statischer Elektrizität kontrolliert. Eigene Messungen und Erfahrungen besagen, dass in der freien Natur die negative Elektrizität im allgemeinen eine ausgleichende und regulierende Kraft darstellt. (s. Gewitter). Hierdurch ist auch nach meiner Ansicht die günstige biologische Wirkung der negativen Elektrizität zu erklären.

PRELIMINARY RESULTS WITH ELECTRO-AEROSOL-THERAPY IN RESPIRATORY DISEASES

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PRELIMINARY results with electro-aerosol therapy (E.A.T) in 200 respiratory patients from three electro-aerosol clinics are described. Some of the characteristics and phenomena of E.A.T. were discussed in connection with brief case histories. Results of space charge potential measurements and air ion counts in an electro-aerosol clinic were reported and their significance for an effective application of E.A.T. explained. The beneficial effects of E.A.T. in respiratory diseases could be confirmed.

VARIOUS PHYSIOLOGICAL AND PATHOLOGICAL PHENOMENA

SEASONAL VARIATIONS IN MORTALITY

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Abstract — A study has been made of the seasonal variations in mortality. The hypothesis is suggested that the magnitude of seasonal fluctuations reflects the magnitude of environmental influences. Mortality data have been collected for areas lying in (1) different hemispheres, (2) within the same hemisphere but different latitudes, and (3) areas within the United States having different climates. These data have been examined over time by age, sex and race and, when possible, by major causes of death. The historical trends of the patterns of the mortality curve are graphically presented. Effects of rural or urban area of residence are shown using Puerto Rico as an example. The hypothesis stated above cannot be properly tested without more complete analysis.

Zusammenfassung — Der Autor hat die Saisonschwankungen in der Sterblichkeit untersucht. Die Hypothese wird diskutirt, dass die Grösse dieser Schwankungen von der Grösse des Einflusses der Umwelt abhängt. Sterblichkeitsziffern für Gebiete: (1) in verschiedenen Hemisphären, (2) in derselben Hemisphäre aber auf verschiedenen Breiten, und (3) Regionen in den Vereinigten Staaten mit verschiedenen Klimaten sind über mehrere Zeitperioden untersucht worden mit Bezug auf Alter, Geschlecht und Rasse der Personen und, wenn möglich, hinsichtlich der wichtigsten Todesursachen. Die historische Richtung der Variationen in der Mortalitätskurve wird graphisch dargestellt. Am Beispiel von Puerto Rico werden die Folgen eines städtischen oder ländlichen Wohnortes gezeigt. Die Hypothese kann ohne eine gründlichere Analyse nicht ausreichend geprüft werden.

Résumé — On a étudié les variations saisonnières de la mortalité. Partant de là, l'auteur propose l'hypothèse suivante: l'importance de ces variations dépend de l'importance de l'influence du milieu ambiant. Il a comparé les chiffres de mortalité provenant de régions différentes: 1) régions situées dans les deux hémisphères, 2) régions situées à des latitudes différentes mais dans le même hémisphère, 3) des zones des Etats-Unis placées sous des climats différents. Les chiffres ainsi recueillis ont été comparés entre eux en les différenciant par périodes et en tenant compte de l'âge, du sexe et de la race des individus et, dans la mesure du possible, des faits ayant entraîné la mort. L'évolution dans le temps de la pente des divers segments de la courbe de mortalité est reportée graphiquement. Les effets d'un habitat urbain ou campagnard sont démontrés au moyen de l'exemple de Puerto Rico. L'hypothèse formulée n'est pas suffisamment établie sans analyse plus poussée.

INTRODUCTION

In his *Airs, Water and Places*, Hippocrates noted the close affinity between weather and climate, and mortality. This phenomenon has, since that time, commanded frequent investigation and study. Gray (1926), Huntington (1930), Chang (1962), Kosambi and Raghavachari (1954), Moine (1955), and Keutzer (1957), to mention a few, are among those who have investigated it in this century. Many diseases of mankind, such as respiratory and circulatory diseases as well as infectious and parasitic diseases, are affected by seasonal variation in weather. By contrast, cancer is a disease whose mortality patterns exhibit little or no seasonal variation.

Many processes have been suggested to account for the association of weather variations and morbidity and mortality patterns. These range from the influence of temperature variations (Gover, 1938) to, in recent years, air pollutants such as "smog" and ozone (Mills, 1957). Pollutants in combination with natural meteorological phenomena have been suggested, for example, by Carey *et al.* (1958) who state that an excess number of deaths occurring during a foggy period over the number of deaths expected in a similar fogless period is "a rough but reliable indication of the lethal effects of air pollution on man."

This paper will present observations on changes in adjusted monthly mortality for all causes and selected causes for countries in different latitudes and for countries and selected places within similar latitudes. The formal hypothesis is suggested that seasonal mortality variations indicate an effect of environment, and by inference, a preventable factor in mortality. The preventable factor might be the effect of heat, cold, humidity; it might be living agents whose life cycles respond to any of the above influences, or to the intensity or duration of sunlight; it might be environmental pollution or it might be related to other environmental processes.

In addition to seasonal fluctuations, there are long-term trends in mortality. Advances in social organization, and in the fields of medicine and public health have greatly reduced the impact of diseases which even a few generations ago were major contributors to mortality. Greater abundance and better distribution of food, improved sanitation, modern refrigeration and stringent laws and social practices governing the handling and processing of food are probably responsible for the lessened mortality from gastrointestinal diseases. Likewise, the development and use of sera and vaccines have, in some countries, nearly eradicated or lessened substantially the mortality from some of the infectious diseases. These are examples of what is meant by preventable factors in mortality.

METHODS

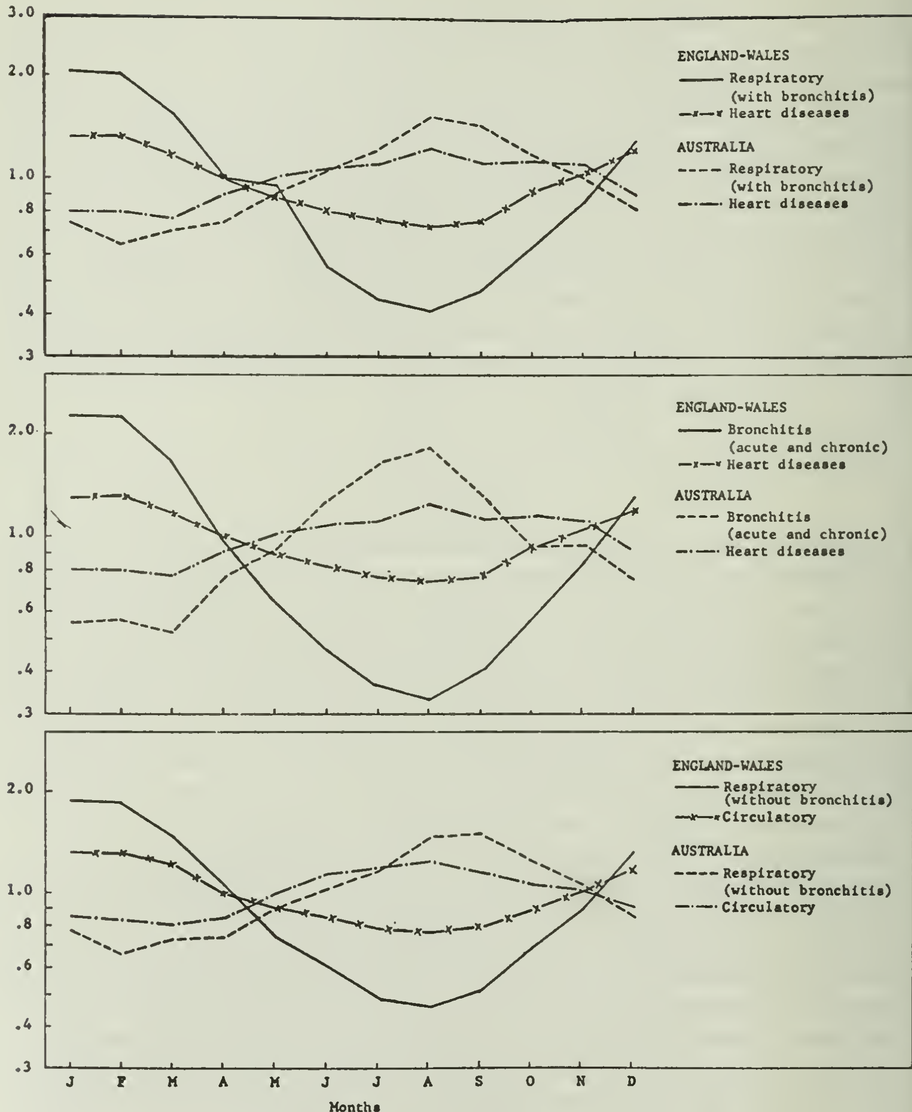
Mortality data have been collected from vital records registries for Australia, England and Wales, Sweden, the United States, Hawaii, California, Michigan, New York, Arizona, New Mexico, Puerto Rico, and the cities of Los Angeles and

Chicago. For Australia, England and Wales and Sweden, the span of years has been grouped in triads spaced approximately at ten year intervals; for the others, triads, dyads and single years have been used. For convenience, data have been presented by month. Presentation by week or by season also could be used; the former could be expected to show more effect of random fluctuation, and in the latter, the choice of periods to represent season would be difficult. In this paper we present the ratios of the mean daily number of deaths for each month to the mean daily number of deaths for the 1-, 2-, or 3-year period. An index of the fluctuations for a given period and cause may be given by the ratio of observed deaths for the month with the greatest mortality to the number of deaths that would be expected if there were no seasonal variation. Particular attention has been given to circulatory and to respiratory diseases, where these data have been available; otherwise, total mortality has been used. Data are analyzed also by race, sex, and urban versus rural residence.

FINDINGS

One effect of seasonal variations in mortality is found in comparing data from the Northern and the Southern hemispheres; the curves are about six months out of phase. The months of June, July, and August in the Southern hemisphere are the winter months, and it is in this period that excess mortality occurs. Figure 1 reflects not only this phenomenon but also the higher amplitude of fluctuations for respiratory diseases compared to circulatory diseases in England and Wales, and the greater fluctuation for England and Wales, compared to Australia. These phenomena persist over a 30-year span. Figure 2 illustrates the fluctuations for circulatory diseases from England and Wales, Hawaii, and Los Angeles County. Australian data have been plotted on the same graph for contrast.

For any given disease, the pattern of seasonal variation may be considered as an epidemiologic characteristic, and short of changes in the conditions affecting its epidemiology, this pattern may be expected to remain stable from year to year. The extent to which any given disease affects the seasonal pattern for all causes of death depends, of course, upon the proportion that this disease entity and its seasonal fluctuation bears to all causes of death. There are some major causes of death, however, which have little or no systematic seasonal deviation and, therefore, have a minimal effect upon the seasonal pattern observed for all causes of death. Cancer is one such disease (Collins, 1953). Respiratory and circulatory diseases, on the other hand, have marked seasonal variations and as major contributors to all causes of death have a substantial effect upon the seasonal fluctuations of the total mortality curve. When respiratory and circulatory diseases are considered as major contributors to total mortality, it should be noted that the contribution of seasonal variations to respiratory diseases exceeds that for circulatory diseases. For Sweden, the monthly proportionate mortality for



The plotted points represent the ratio $\frac{\text{mean number of daily deaths for month}}{\text{mean number of daily deaths for entire period}}$.

FIG. 1. Seasonal mortality variations, England–Wales and Australia, respiratory, heart diseases, circulatory 1931–1933

respiratory causes of death varies by about five or six per cent of total monthly mortality over a twenty year span, while the variation in proportionate mortality for circulatory causes of death amounts to about 3 per cent in 1930–32, and even less in 1950–52 (Table 1). For England and Wales, for the period 1921–23 to 1951–53,

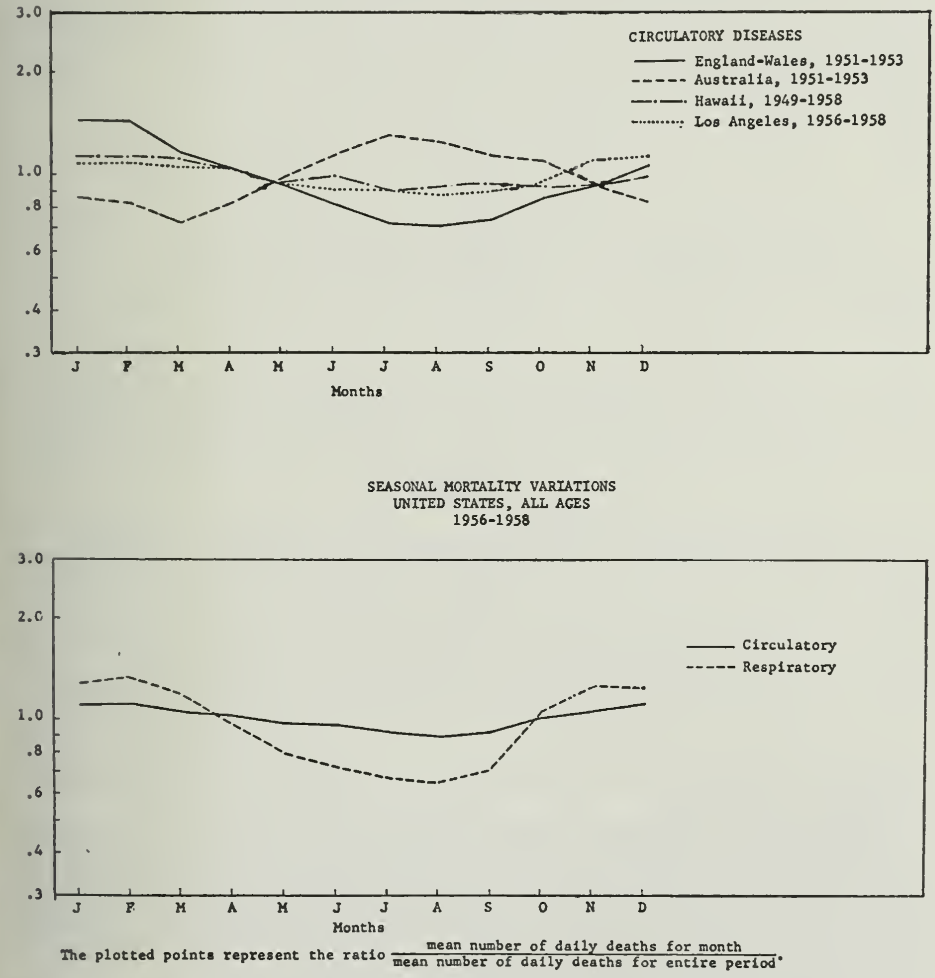


FIG. 2. Seasonal mortality variations by selected geographical locations, circulatory diseases. Seasonal mortality variations United States, all ages 1956–1958

the monthly proportionate mortality for respiratory causes of death varies by between eleven and seventeen per cent of total monthly mortality, while the variation for circulatory causes ranges from about $2^1/_2$ to $3^1/_2$ per cent (Table 2).

Table 1. Per cent of Contribution of Respiratory and of Circulatory Deaths to Deaths, All Causes, for Selected Periods, by Month, Sweden

	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
						1930–32						
Deaths, all causes:	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Resp.	11.6	11.2	10.1	11.4	10.4	7.9	6.1	5.0	6.4	7.6	8.2	9.6
Circ.	19.9	19.0	20.0	19.6	19.9	20.4	20.8	20.7	21.7	22.3	21.2	21.9
						1940–42						
Deaths, all causes:	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Resp.	9.8	10.6	8.7	8.1	7.4	5.5	5.2	4.4	4.7	5.4	6.1	6.8
Circ.	28.1	27.8	27.5	27.6	26.9	26.6	26.9	26.8	27.2	28.2	27.6	27.8
						1950–52						
Deaths, all causes:	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Resp.	8.3	6.4	6.4	5.8	5.0	4.3	4.0	3.4	3.7	4.0	4.7	5.2
Circ.	33.7	33.6	32.7	32.6	31.3	31.5	31.6	31.3	32.0	32.9	32.8	33.7

A similar pattern is shown for respiratory and circulatory mortality for the United States (data for 1956–58).

It readily can be shown that long-term changes have taken place in the seasonal patterns of the total mortality curve. The Metropolitan Life Insurance Company (Statistical Bulletin, 1955) has stated that improvements in sanitation in New York and Chicago in the past 50 years or so have brought about a complete shift in the maximum mortality from summer to winter.

In this paper, this shift has been illustrated by utilizing data collected for the city of Chicago for the period 1867–1925. Figure 3 shows the striking alteration in the monthly mortality pattern for this period. Tables 3 and 4 present the historical course of selected causes of death for the same period, and the per cent of contribution each makes to total mortality, by month as well as the annual contribution.

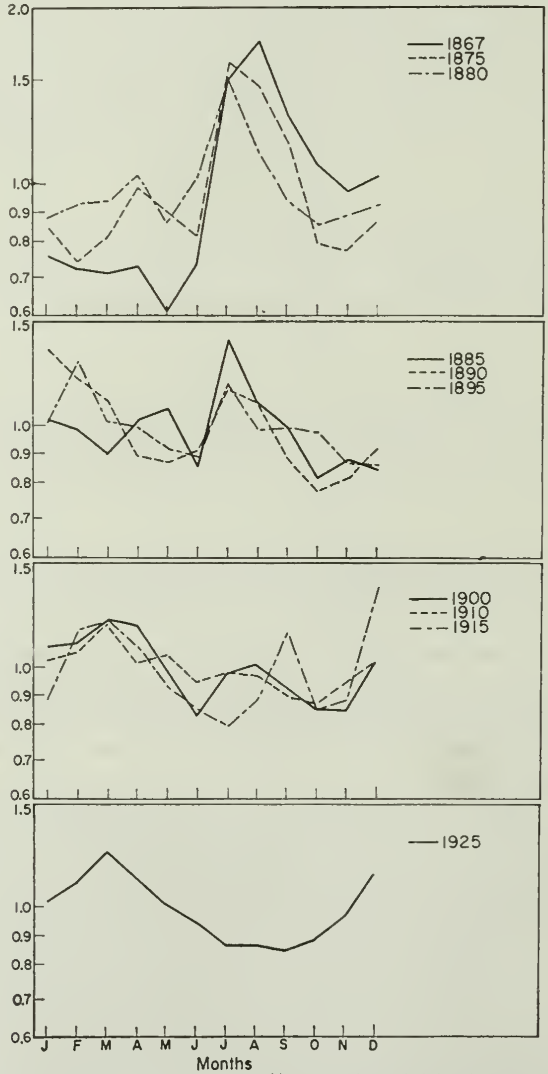
Table 2. Per Cent of Contribution of Respiratory and of Circulatory Deaths to Deaths, All Causes, for Selected Periods, by Month, England–Wales

	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
						1921–23						
Deaths, all causes:	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Resp.	21.5	21.7	19.9	19.4	16.7	13.1	10.7	9.3	10.3	12.3	17.7	20.7
Circ.	14.4	14.7	15.1	14.8	15.5	15.9	16.3	17.0	16.2	16.5	17.0	16.5
						1931–33						
Deaths, all causes:	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Resp.	17.5	17.3	15.2	11.8	9.5	7.9	6.7	6.3	7.1	8.9	9.5	14.0
Circ.	24.9	24.7	26.0	25.6	26.5	26.4	26.3	25.8	26.3	27.1	23.9	27.6
						1951–53						
Deaths, all causes:	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Resp.	23.4	21.4	14.7	11.0	8.1	6.5	5.7	5.6	5.9	8.5	9.6	13.8
Circ.	35.4	36.1	37.4	37.5	38.4	36.1	35.1	34.8	35.2	36.1	36.8	37.2

The major contribution of the digestive diseases for the period 1867–1895 clusters generally in the period June–September and represents a range of 78 to 90 per cent of all deaths due to these diseases occurring in any given year; in other words, these diseases take their highest toll in the warm months. Contrariwise, in the same period the contribution of respiratory diseases clusters about the months October through May and represents a range of 79 to 88 per cent of all mortality resulting from these diseases in any given year; these diseases take their highest toll in the cold months.

It is important, however, to note their per cent of contribution to total mortality on an annual basis, over a span of time. In the period 1867–1890, there was a decrease in digestive diseases with a corresponding increased contribution of respiratory diseases. (During the period 1890–1895, there was a decline in the relative contribution of respiratory diseases.) After 1895, the Chicago Board of Health no longer listed digestive diseases as a principal cause of death. Though still listed, infective and parasitic diseases have become neglible contributors by 1925. A different definition applies to these diseases in the period 1900–1925 than that applying to the period 1867–1895 (Footnotes Table 4). The altered seasonal mortality curve for 1925 was clearly due to the lessening influence of diseases whose toll was taken in the summer months, on the one hand, and the increase of respiratory diseases, whose toll was taken in the winter months.

Respiratory diseases themselves contribute heavily to mortality in the cold months, and also play a major role in determining the shape of the seasonal mortality curve for other conditions, presumably because respiratory conditions tend to contribute to the mortality of persons suffering from other serious chronic



The plotted points represent the ratio $\frac{\text{Mean number of daily deaths for month}}{\text{Mean number of daily deaths for entire period}}$

Fig. 3. Seasonal mortality variations, deaths, all causes, Chicago

Table 3. Per Cent of Contribution of Selected Causes of Death to Deaths, All Causes, by Month, Chicago, 1867-1895

Nomenclature	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total Deaths	Per cent of all causes (annual)
							1867							
Digestive*	1.3	0.4	—	2.5	0.4	3.9	36.3	36.9	26.2	12.4	2.1	1.2		
	(4)	(1)	(—)	(7)	(1)	(11)	(217)	(257)	(133)	(53)	(8)	(5)	(697)	15.0
Cancer	0.7	1.2	0.7	0.7	1.2	1.1	0.4	0.7	0.8	1.6	1.9	1.0		
	(2)	(3)	(2)	(2)	(3)	(3)	(3)	(5)	(4)	(7)	(7)	(4)	(45)	1.0
							1875							
Digestive*	1.1	.4	.5	4.0	1.7	9.4	42.0	34.9	25.7	5.4	1.0	0.5		
	(6)	(2)	(3)	(26)	(10)	(50)	(492)	(344)	(196)	(29)	(5)	(3)	(1,166)	14.8
Cancer	1.8	1.6	1.6	.9	2.2	2.1	1.3	1.4	1.4	1.9	1.4	1.5		
	(10)	(7)	(9)	(6)	(13)	(11)	(15)	(14)	(11)	(10)	(7)	(9)	(122)	1.5
							1880							
Digestive*	0.6	0.5	0.1	0.4	2.3	16.1	27.0	18.2	7.6	3.2	0.9	0.2		
	(5)	(4)	(1)	(4)	(18)	(144)	(362)	(186)	(62)	(25)	(7)	(2)	(820)	7.9
Cancer	1.3	1.3	1.8	2.1	2.1	.9	1.2	1.2	1.1	1.6	2.3	2.2		
	(10)	(10)	(15)	(19)	(16)	(8)	(16)	(12)	(9)	(12)	(18)	(18)	(163)	1.6
							1885							
Digestive	0.6	0.6	0.7	2.5	5.2	6.1	23.9	20.9	8.5	2.4	0.6	1.3		
	(7)	(6)	(7)	(26)	(59)	(54)	(357)	(248)	(89)	(21)	(5)	(12)	(891)	7.1
Cancer	2.7	1.9	2.1	2.1	2.0	1.9	1.7	1.3	1.3	2.1	2.3	2.7		
	(30)	(18)	(20)	(22)	(23)	(17)	(26)	(16)	(14)	(18)	(21)	(24)	(249)	2.0

Nomenclature	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total Deaths	Per cent of all Causes (annual)
							1890							
Digestive*	1.2	2.0	0.9	1.1	1.3	4.6	24.8	17.8	9.4	2.7	0.8	0.3		
	(30)	(41)	(18)	(18)	(21)	(76)	(532)	(363)	(148)	(39)	(12)	(5)	(1,303)	6.0
Cancer	1.6	1.6	1.6	2.4	2.5	2.2	1.9	2.1	2.2	2.4	2.4	2.2		
	(39)	(32)	(33)	(38)	(40)	(37)	(40)	(45)	(46)	(38)	(36)	(37)	(461)	2.1
							1895							
Digestive*	0.5	0.3	0.3	0.6	1.6	10.2	22.2	16.1	13.8	3.2	0.9	0.6		
	(10)	(7)	(6)	(12)	(31)	(180)	(542)	(329)	(279)	(64)	(15)	(11)	(1,476)	6.1
Cancer	2.4	2.3	2.4	2.7	3.2	3.2	2.7	2.8	3.1	2.9	2.8	3.7		
	(50)	(54)	(50)	(53)	(61)	(57)	(67)	(57)	(62)	(58)	(48)	(65)	(682)	2.8

* Includes cholera infantum and diarrhea.

Table 4. Per Cent of Contribution of Selected Causes of Death to Deaths, All Causes, by Month, Chicago, 1867–1925

Nomenclature	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total Deaths	Per cent of all causes (annual)
							1867							
Infective-Parasitic*	31.8	29.8	25.4	24.5	28.6	25.4	11.1	10.8	14.6	18.5	24.9	27.6		
	(95)	(76)	(71)	(68)	(69)	(72)	(66)	(75)	(74)	(79)	(93)	(113)	(977)	21.0
Respiratory+	7.7	11.4	7.9	11.9	8.3	1.9	2.3	0.9	2.2	5.6	12.3	14.7		
	(23)	(29)	(22)	(33)	(20)	(5)	(14)	(6)	(11)	(24)	(46)	(60)	(293)	6.3
							1880							
Infective-Parasitic*	32.6	30.8	29.2	22.8	22.2	19.8	15.4	19.7	28.2	30.6	24.3	24.5		
	(256)	(230)	(243)	(203)	(171)	(177)	(207)	(201)	(229)	(235)	(187)	(203)	(2,542)	24.3
Respiratory+	14.9	16.6	22.8	25.7	18.3	9.5	3.7	7.1	9.9	15.6	19.0	19.2		
	(117)	(124)	(190)	(229)	(141)	(85)	(50)	(72)	(80)	(120)	(146)	(159)	(1,514)	14.5
							1895							
Infective-Parasitic*	20.9	15.2	16.4	17.1	16.6	16.0	14.1	17.5	18.6	26.2	25.6	22.8		
	(437)	(358)	(349)	(340)	(312)	(283)	(343)	(356)	(374)	(530)	(441)	(403)	(4,526)	18.7
Respiratory+	22.9	29.5	24.3	22.0	16.3	9.5	5.7	6.7	6.8	10.4	14.3	13.0		
	(478)	(694)	(516)	(437)	(308)	(169)	(140)	(137)	(138)	(210)	(247)	(230)	(3,704)	15.3
							1910							
Infective-Parasitic*	4.3	4.0	3.5	4.0	5.0	3.7	3.9	3.5	4.2	5.7	7.5	5.7		
	(126)	(108)	(118)	(111)	(147)	(97)	(108)	(96)	(103)	(141)	(194)	(167)	(1,526)	4.6
Respiratory+	19.1	20.8	22.0	18.8	18.9	16.3	8.3	6.8	7.4	10.2	17.0	21.9		
	(558)	(562)	(730)	(525)	(559)	(422)	(230)	(186)	(182)	(252)	(442)	(638)	(5,286)	15.8

Nomenclature	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total Deaths	Per cent of all causes (annual)
	1925													
Infective-Parasitic†	1.7 (50)	0.6 (18)	1.3 (46)	1.1 (36)	1.4 (40)	1.3 (34)	0.8 (21)	1.0 (24)	1.1 (25)	1.2 (31)	1.5 (41)	1.2 (40)	(412)	1.2
Respiratory†	11.3 (338)	12.1 (351)	14.0 (504)	12.2 (389)	9.6 (285)	6.8 (180)	4.7 (119)	4.9 (123)	4.1 (98)	5.9 (153)	9.6 (263)	8.1 (272)	(3,075)	9.0

* Includes measles, whooping cough, dysentery, typhoid, consumption, diphtheria and scarlet fever.
\+ Includes pneumonia, bronchitis and croup.
† Includes diphtheria, typhoid and scarlet fever.
†† Includes pneumonia only.

diseases. Collins (1953), for example, has shown that during epidemics of influenza, excess mortality (i.e. mortality-greater than expected, using seasonal corrections) also occurs from a variety of conditions other than influenza or pneumonia. In studying influenza and pneumonia epidemics from 1918 to 1947, he found that for the 1918–1919 episode, maternal deaths were exceptionally high. They were moderately high, also, in 1920. Through the entire period 1918 to 1947, more of the excess deaths from causes other than influenza and pneumonia were credited to heart diseases than to any other diseases considered. In the period 1918–29, excess deaths due to nephritis were high during epidemic periods. For the period 1922–1947, there was an excess of deaths due to diabetes. Deaths due to bronchitis likewise exhibited an excess for the period 1918–1929.

Climate contributes its share to the phenomenon of seasonal mortality variations in the way it affects the duration and character of the seasons. In regions such as Hawaii and California, for example, where there is an absence of wide variations between winter and summer temperatures, the seasonal mortality pattern still remains evident; however, the fluctuations are not as great as those for Australia, England and Wales, or Sweden. Seasonal mortality patterns for California have been compared to those for Michigan, New York, Arizona and New Mexico, as well as for the United States as a whole. These states were chosen as being substantially different as to climate, weather variations, and humidity. New York is coastal; Michigan is inland; but both have distinct seasonal variations with wide temperature fluctuations. Arizona and New Mexico are similar in that they are semi-arid, and their winters are not as severe as those in New York or Michigan. Examination of these patterns revealed that the peak mortality for California, Arizona, and New Mexico is reached generally one or two months earlier than the peaks for Michigan and New York. The earlier appearance of maximal monthly mortality for these states raises the question as to whether the onset of cold weather may have a greater effect than the persistence of cold weather in these areas. Race and sex contributed little to the seasonal mortality patterns.

Moriyama and Herrington (1938), utilizing data that represented average mortality rates in each of the states in the United States Registration Area for the ten year period 1921–30, (there were 35 in 1921 and 48 in 1930), studied the relationship of diseases of the cardiovascular and renal systems to climate and to a socio-economic group of factors, namely degree of urbanization, per capita income, and the proportion of Negroes in the population.

They found that the socio-economic factors have a much more pronounced effect (in a ratio of approximately 3:1) than do the climatic factors. Further, they found in the more highly urbanized and prosperous areas that the rates for circulatory diseases tend to vary in direct proportion to the degree of urbanization and prosperity; in rural and less prosperous areas, the high rates tended to be associated with the percentage of Negroes in the population.

In order to explore this relationship, mortality data for Puerto Rico were examined. These data were in a form that made possible a race-residence study. For the most part, the mortality peak in the rural areas occurs during the winter months while that for the urban areas occurs during the summer months. By 1938–41 the patterns have become similar (Fig. 4). This shift may be related to the fact that infectious and parasitic diseases, and digestive diseases are heavy contribu-

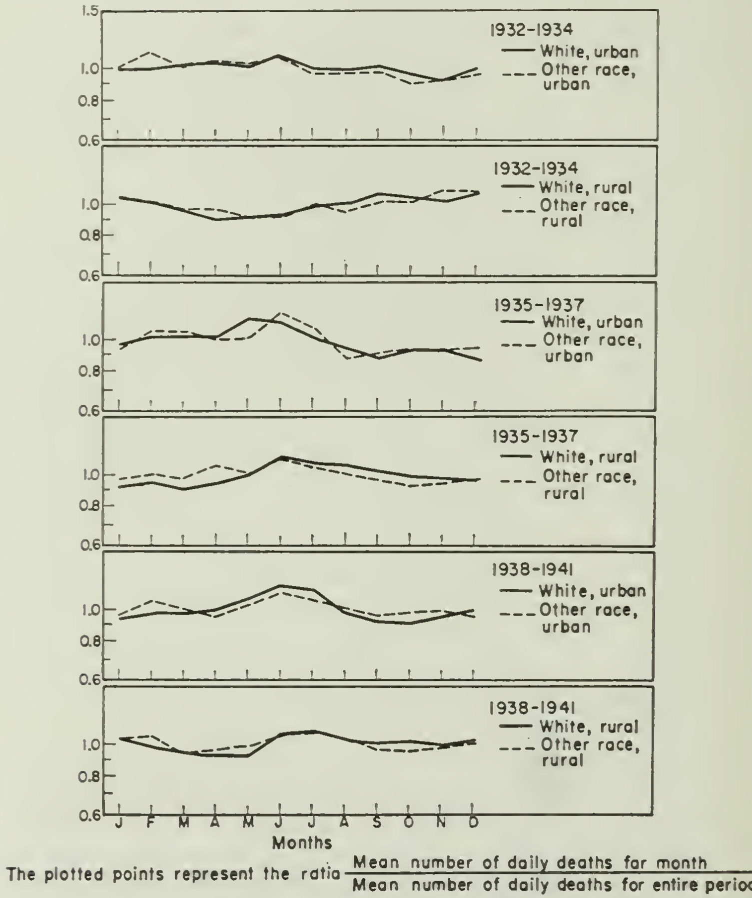
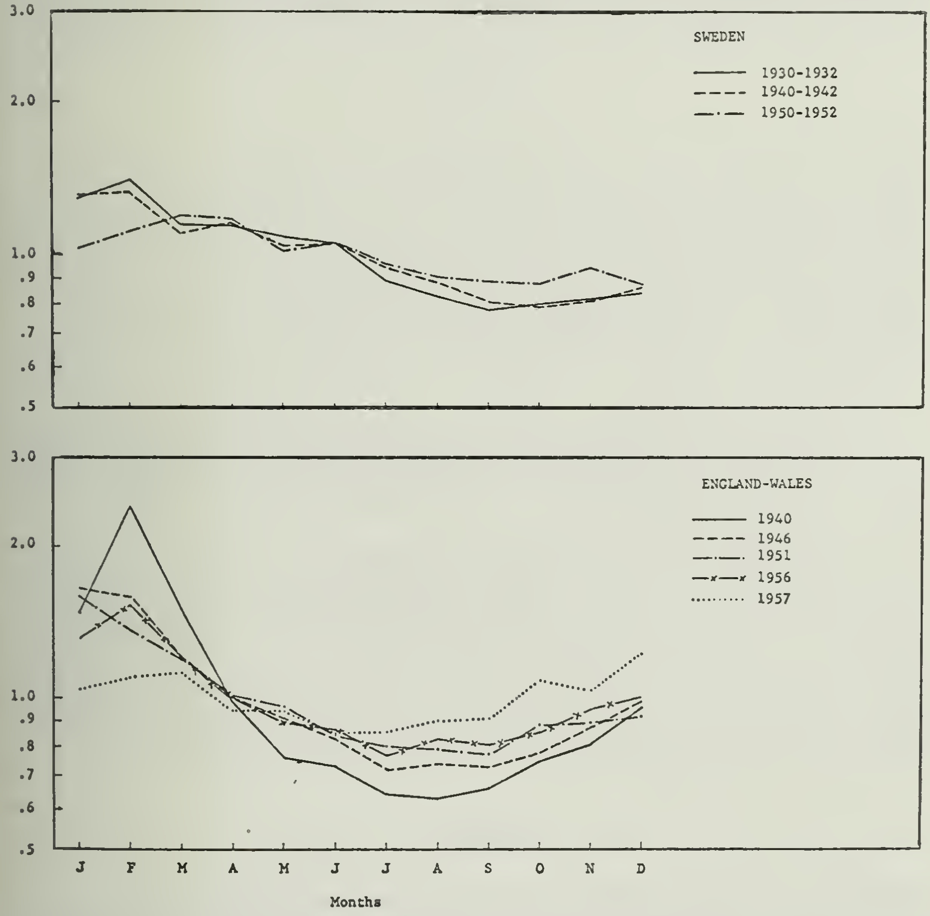


FIG. 4. Seasonal mortality variations, Puerto Rico Deaths. All causes, by race and residence – urban vs. rural residence

tors to total mortality. Their contribution, while decreasing over time, still represented an important part of the mortality pattern as late as 1950–51. These two cause groups accounted for about half the total deaths in 1932–34 and about a third in 1950–51.

As has been stated earlier, seasonal variation may be considered an epidemiological characteristic of a disease. For the purpose of contrast with the respiratory and circulatory diseases, attention has been given to the category of infectious and parasitic diseases. It is reasonable to expect that these diseases would have an established seasonal characteristic. Figure 5 depicts the course of these



The plotted points represent the ratio $\frac{\text{mean number of daily deaths for month}}{\text{mean number of daily deaths for entire period}}$.

FIG. 5. Seasonal mortality variations, Sweden and England and Wales, infectious-parasitic diseases

diseases for England and Wales and Sweden. It will be noted that the curves for each of these countries, over time, have "flattened". The seasonal characteristic has not, however, disappeared.

As a final step in the investigation of environmental implications of seasonal variations in mortality, attention was given to a cause of mortality not necessarily associated with physical disabilities which cause death. Suicide was chosen for illustration, using Swedish mortality data for the period 1930–1952. Here again a seasonal pattern is found. The data reveal that the maximum suicide frequency for Sweden for the period studied occurs in the warm months.

DISCUSSION

Mortality data represent a readily available and attractive source of information for use in the investigation of the effect of meteorological and other environmental factors on human health. They have been found to be most useful, for example, in studying the health effects of air pollution on human populations. In order to draw reasonable conclusions from mortality data concerning biometeorologic effects on human health, a number of problems present themselves:

(1) Nosological Validity. While in most countries the date of deaths is reported accurately, and the numbers of deaths can be relied upon, cause of death often is not uniformly reported;

(2) Specificity. Generally, no set of mortality data reflects the specific effect of any meteorologic or environmental variable singly or in combination. Traditionally, what is reflected is the end result of a great variety of influences operating over varying time spans;

(3) Statistical and Analytic Methods. Existing statistical and analytical methods often are not adaptable to the type of data being studied. It thus becomes necessary to develop more suitable statistical tools (Hechter and Goldsmith, 1961; Bliss, 1958). Nonparametric methods, too, should be of considerable use in situations of this sort, where the underlying distributions are not known and there is little reason to suspect normality. Still newer statistical concepts and techniques might have to be developed for analyzing some aspects of this problem.

SUMMARY

Seasonal variations in mortality patterns have been presented. Environmental and preventive implications have been discussed briefly. No attempt has been made to statistically analyze the data. Attention is now being directed to the development of more pertinent and sensitive statistical methods to be utilized in the analysis of the data.

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INFLUENCES MULTIPLES DU CLIMAT SUR LA POTASSÉMIE ET LA TOLÉRANCE AU POTASSIUM CHEZ L'HOMME*

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Abstract — Plasma potassium of Indians living in Madras is subject to seasonal variations of short duration. These variations seem related to sudden changes of temperature during spring and autumn. Plasma potassium of Indian and European students is, furthermore, higher in tropical climate than in Europe. On the other hand, the mineralocorticoid activity of adrenal cortex estimated by means of K tolerance tests, is progressively stimulated by cold climate and depressed by tropical climate over long periods of time. Multiple influences of climate on these parameters are discussed.

Zusammenfassung — Plasma-Kalium der Indier in Madras unterliegt jahreszeitlichen Veränderungen von kurzer Dauer. Diese Veränderungen scheinen in Zusammenhang zu sein mit den schnellen Temperaturveränderungen, die im Frühling und Herbst beobachtet werden. Anderseits ist das Plasma-Kalium von indischen und europäischen Studenten höher im tropischen Klima als in Europa. Die Kaliumtoleranzprüfung hat gezeigt, dass auf lange Sicht die Mineralocorticoid-Aktivität der Nebennieren in der gemässigten Zone erhöht und der tropischen Zone vermindert ist. Die zahlreichen Einflüsse des Klimas auf diese Parameter werden diskutiert.

Résumé — La potassémie de sujets indous vivant à Madras subit des fluctuations saisonnières de courte durée. Ces fluctuations semblent en rapport avec les changements brusques de la température observés au printemps et en automne. Le K plasmatique de groupes d'étudiants indous et européens est, d'autre part, plus élevé en climat tropical qu'en climat tempéré. Enfin, la fonction minéralotrope de la glande surrénale, estimée par le test de tolérance au K, est stimulée à longue échéance par le climat tempéré et déprimée par le climat tropical. On discute enfin les influences multiples du climat sur ces paramètres.

INTRODUCTION

Au cours de ces dernières années, nous avons étudié l'influence du climat, des saisons et de la race sur le potassium plasmatique et la tolérance au potassium de populations indiennes et européennes. Le test de tolérance au K était utilisé pour estimer la fonction minéralotrope de la glande corticosurrénale.

L'analyse des résultats acquis jusqu'ici est exposée dans le présent travail.

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MÉTHODES

Tous les sujets testés sont en bonne santé et de sexe masculin. Ils sont âgés de 20 à 35 ans, à l'exception de 3 sujets âgés de 40 à 45 ans.

Le sang est prélevé à la veine, le matin à jeun. Il est recueilli sur héparine et immédiatement centrifugé. Le dosage du K est fait sur le plasma par photométrie de flamme et les résultats sont exprimés en mg de K par 100 ml de plasma. Les mêmes solutions minérales standards ont été utilisées en Inde et en Europe. A titre de contrôle supplémentaire, des échantillons de plasma, transportés en tube de polyéthylène scellés, ont été dosés à la fois en Inde et en Europe. L'erreur sur le dosage est de ± 0.3 mg%.

Le test de tolérance au K est exécuté de la manière suivante: quatre échantillons de sang sont prélevés, l'un à jeun, les autres 20, 40 et 60 min après ingestion orale d'une solution de KCl à raison de 20 mg de sel dans 2 ml d'eau par Kg de poids corporel. Le maximum d'augmentation du K plasmatique se situe généralement à la quarantième minute. Chez 12 sujets, après ingestion d'eau sans KCl, on observe une augmentation moyenne de potassémie égale à 0.46 mg %.

Les moyennes des résultats sont comparées au moyen du test.

RÉSULTATS

1. Variations Saisonnières du K *Plasmatique en Inde*

L'étude des variations saisonnières du K plasmatique a été faite à Madras, uniquement sur des groups d'étudiants et d'ouvriers indiens. Aucune différence notable en relation avec la profession des sujets n'a été décelée.

En octobre, les sujets ont tous été testés vers la fin du mois, au plus fort de la mousson d'automne. En janvier-février et mars-avril, les examens ont eu lieu pendant quelques jours, à la fin du premier mois et au début du suivant; les données relatives à ces mois ont donc été groupées. Dans les autres cas, les examens ont été répartis pendant toute la durée du mois (tableau 1).

Les températures effectives ont été calculées à partir des données de température et d'humidité atmosphériques relevées par le Régional Meteorological Centre de Madras, au moyen d'abaques dressées par Ferderber and Houghten (1941). Les moyennes mensuelles des températures atmosphériques calculées à partir des moyennes par 24 heures, présentent des variations parallèles à celles des températures effectives.

Un travail préliminaire (Henrotte et Krishnaraj, 1962) montrait l'existence d'une diminution de potassémie pendant la mousson. Par ailleurs, des valeurs très hautes sont observées en mai, pendant la période la plus chaude. La figure 1 montre cependant que la potassémie semble surtout affectée par les changements de température plutôt que par la température elle-même. Nos données sug-

Tableau 1

Madras 1960 – 1961	$\bar{K}$ plasmatique, mg %				Température effective °C
	n	*m*	*S*	*SE*	
Août	27	18.42†	2.47	0.48	27.1
Septembre	24	17.17	2.15	0.45	26.4
Octobre }	29	16.21†	1.45	0.27	24.4
Novembre }					24.0
Décembre	17	18.85†	2.48	0.62	23.8
Janvier }	26	17.99	1.67	0.33	23.3
Février }					24.4
Mars }	7	17.43*	2.09	0.85	26.1
Avril }					27.8
Mai	16	19.09*	1.55	0.40	28.2
Juin	14	18.03	2.11	0.58	27.3

Potassium plasmatique de sujets Indous;
n = nombre de sujets, m = moyenne, S = écart-type, SE = erreur standard.
Les moyennes mensuelles des températures effectives sont indiquées en °C.
Moyennes significativement différentes.
$P < 0.05$* $P < 0.001$†.

gèrent l'existence d'une corrélation négative entre la potassémie de nos groupes humains et le module de la première dérivée de la courbe température temps. Dans le graphique, la dérivée a simplement été obtenue en calculant la différence, prise

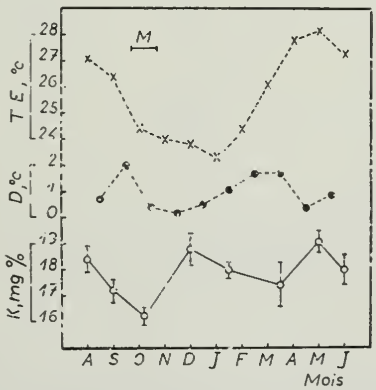

Fig. 1. Graphique supérieur: températures effectives calculées à partir des valeurs de température et d'humidité; moyennes mensuelles en °C.
Graphique intermédiaire: différences, prises en valeur absolue, entre les moyennes mensuelles du graphique supérieur
Graphique inférieur: moyennes et erreurs standard du K plasmatique de sujets Indous
M: période de la mousson

en valeur absolue, entre les températures des mois successifs. D'autres données, non publiées, concernant les variations saisonnières de la vitesse de sédimentation montrent également l'existence de minima en octobre-novembre et mars-avril.

2. *Variations Climatiques du* K *Plasmatique et de la Tolérance au* K, *en Inde et en Europe*

Les variables. La tolérance au K a été déterminée un été (juin et août) à Madras sur 16 étudiants indous tamouls et 16 sujets de race blanche (Français, Anglais et Nord-Américains) et en hiver (décembre, janvier et février) à Liège et à Paris sur 18 étudiants indous et 20 étudiants belges. Signalons que 12 des étudiants belges testés en janvier (Henrotte, Ranganathan et Krishnamurthi, 1960) ont une tolérance au K nettement meilleure que celle des 8 autres sujets belges testés subséquemment en février. Ce résultat suggère l'existence de fluctuations saisonnières. Les différences ne sont toutefois pas significatives et dans le présent travail les 20 étudiants belges sont considérés comme formant un seul groupe homogène.

Tableau 2

Groupes	*I*		*M*		*D*	
En Inde	*m*	*S*	*m*	*S*	*m*	*S*
16 Indous	17.82	1.29	20.26	1.76	2.43	1.31
16 Européens	17.83	1.26	19.67	1.20	1.84	1.43
En Europe						
18 Indous	16.52	0.97	18.43	2.30	1.91	2.31
20 Européens	15.11	1.48	16.83	1.50	1.73	1.79

Test de tolérance au potassium.
I = valeur initiale du potassium plasmatique;
M = valeur maximum atteinte pendant le test;
D = variation maximum du K pendant le test.
Toutes les valeurs sont exprimées en mg pour 100 cm^3 de plasma.

Dans ces quatre groupes, trois paramètres ont été étudiés simultanément: la valeur initiale, I, du potassium plasmatique avant ingestion de KCl, la valeur maximum, M, atteinte par le potassium plasmatique après ingestion de KCl et la différence, D, entre les deux valeurs précédentes (tableau 2). Cinq sujets présentent une courbe de tolérance inversée, c.-à-d. une diminution du K plasmatique à la 20ème et 40ème minute avec retour à la normale à la 60ème minute. Dans ces cas, M est considéré comme égal à la valeur minimum observée et D est négatif. La valeur D, quel que soit son signe, représente donc toujours le maximum de variation de la potassémie par rapport à la valeur initiale.

Pour les sujets résidant en pays étranger, le logarithme, T, de la durée de séjour exprimée en mois, a également été étudié en corrélation avec les autres variables. Les durées de séjour s'échelonnent de 0.5 à 132 mois. Elles sont en moyenne de 9 mois pour les Européens en Inde et de 26 mois pour les Indous en Europe. Les individus qui ont fait plusieurs séjours en pays tropical ou tempéré n'ont pas été retenus.

Le potassium plasmatique à jeun est plus élevé en Inde qu'en Europe et en Europe, il est plus élevé chez les Indous que chez les Européens ($P < 0.01$). Cette dernière différence peut cependant être due à des variations mensuelles; les étudiants indous ont été testés en décembre (Henrotte et Justin, 1963) et les étudiants européens en janvier et février. Il n'existe par contre aucune différence entre les Européens et les Indious examinés en Inde (Henrotte, Ranganathan et Krisnamurthi, 1960).

La tolérance au K de chaque group est estimée par la valeur moyenne de D. Ces moyennes ne peuvent être comparées comme telles puisque la tolérance au K dépend, suivant les groupes, de la valeur initiale de la potassémie ou de la durée de séjour (tableau 3).

Tableau 3

r	Inde		Europe	
	16 Indous	16 Européens	18 Indous	20 Européens
I M	0.672†	0.330	0.200	0.292
I D	−0.076	−0.608*	−0.221	−0.600†
I T	—	0.102	0.089	—
M T	—	0.654†	−0.515	—
D T	—	0.460	−0.550*	—
M $T.I$	—	0.661†	+0.546*	—
D $T.I$	—	0.666†	−0.546*	—

Coefficients de corrélations simples et partielles entre les variables I, M et D, et le logarithme de la durée de séjour T, dans les différents groupes humains considérés au tableau 2.
Seuil de signification: $P < 0.05$*, $P < 0.01$ †

Des recherches antérieures ont montré que l'augmentation de potassémie pendant le test est d'autant plus grande, chez les Européens résidant en Inde, que la durée de leur séjour en climat tropical est plus longue (Henrotte, Krishnamurthi et Ranganathan, 1960). Une relation inverse pour les Indous résidant en Europe a aussi été récemment démontrée (Henrotte et Justin, 1963). Toutefois, dans chacun de ces groupes, nous avions volontairement omis les valeurs de D négatives, c.-à-d. les données relatives aux courbes de tolérance au K inversées. Les corrélations étaient alors les suivantes:

$r_{DT} = 0.659$, ($P < 0.02$) pour 15 Européens en Inde et
$r_{DT} = -0.610$, ($P < 0.01$) pour 17 Indous en Europe.

Ces corrélations deviennent plus faibles, $r_{DT} = 0.460$ et -0.550, si l'on inclut dans la statistique les valeurs des sujets présentant une courbe de tolérance inversée (tableau 3). Ces sujets sont respectivement au nombre de 3 dans le groupe des Européens en Europe et d'un dans celui des Indous en Europe et des Européens en Inde.

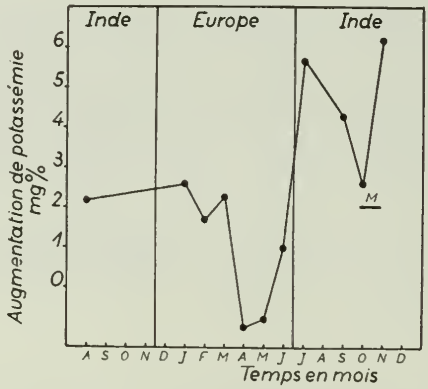

Fig. 2. Augmentation maximum de la potassémie pendant le test de tolérance au K, chez un même sujet, au cours de différents séjours en Inde et en Europe. *M:* période de la mousson

L'examen attentif des données révèle les faits suivants:

1. Les courbes inversées apparaissent chez les individus dont la potassémie initiale à jeun est très élevée par rapport à la moyenne de leur groupe, inversement des valeurs élevées de D correspondent à des potassémies initiales très basses de l'ordre de 13 mg %;

2. Il existe une corrélation significative, r_{ID}, entre la valeur initiale du K et la variation de la potassémie, dans 2 des 4 groupes étudiés (tableau 3). Dans le groupe des Européens en Inde on obtient une corrélation significative entre D et T si on élimine l'influence de la valeur initiale du K en calculant la corrélation partielle $r_{DT.I}$.

Compte tenu des autres facteurs de variations, on peut donc démontrer l'existence d'une relation significative entre la tolérance au K estimée par D ou M et la durée de séjour T. Le petit nombre de données et leur grande dispersion rend illusoire le calcul des équations de régression. Signalons cependant, que la valeur D, extrapolée pour une durée de séjour égale à 24 mois est de 2.29 mg % dans le groupe des Européens en Inde, et de 2.00 mg % dans celui des Indous en Europe. L'augmentation de potassémie pendant le test de tolérance au K serait donc plus grande en Inde qu'en Europe quelle que soit la race des sujets.

Une étude longitudinale, réalisée par l'auteur sur lui-même au cours de voyages en Inde et en Europe, confirme les résultats précédents. Les variations du K plasmatique ont été décrites précédemment (Henrotte et Krishnaraj, 1962); les fluctuations de la tolérance au K estimée par la valeur de D, sont reportées à la fig. 2 La courbe de tolérance au K est moyennement élevée après 2 mois de séjour en Inde; elle s'aplatit rapidement en Europe et devient même légèrement négative pour remonter à des valeurs très élevées en Inde. L'influence du fraichissement de la température pendant la mousson paraît notable.

DISCUSSION

Le K plasmatique chez l'homme présente des variations climatiques importantes. Pendant trois mois d'hiver, en Europe, les moyennes sont plus basses que toutes celles observées pendant une année en Inde, exception faite des valeurs obtenues pendant la mousson d'octobre. Les fluctuations saisonnières observées à Madras montrent l'importance des changements brusques de température au printemps et en automne. Les valeurs obtenues par Sargent et Weinman (1962) à partir de deux groupes différents de 88 soldats américains confirment l'influence du climat sur la potassémie: le groupe testé en hiver a une potassémie moyenne de 16.4 ± 1.6 mg % tandis que la potassémie du groupe d'été est de 17.8 ± 1.8 mg %. Par contre, au Japon, Yoshimura (1958) observe chez 8 sujets, une augmentation de potassémie pendant l'hiver et une diminution l'été. Les causes de ces variations ne sont pas connues.

Si le K plasmatique est généralement considéré comme un mauvais facteur d'estimation de l'activité corticosurrénale (Bloch 1959), la tolérance au K semble au contraire donner des indications précises sur la fonction minéralotrope de cette glande. On sait que la tolérance au K est diminuée dans l'insuffisance surrénale chronique (Zwemer et Truskowski, 1936) et qu'elle est augmentée chez l'individu normal après injection d'acétate de désoxicorticostérone (Leschi, 1951). Dans ce dernier cas, on observe des courbes de tolérance très aplaties ou même inversées. Nos résultats indiquent donc l'existence d'une stimulation de la fonction corticosurrénale par le climat tempéré et de sa dépression par le climat tropical. Contrairement à ce qui est observé pour le K plasmatique, l'influence du climat sur la tolérance au K est relativement lente et semble agir à longue échéance. Aucune différence raciale nette entre Indous et Européens n'est mise en évidence. Les données de Leschi (1951) semblent indiquer que la tolérance au K des Noirs Africains est moins bonne que celle de nos populations européennes et indoues.

Quant à l'influence du régime alimentaire, elle ne paraît pas déterminante. Beaucoup d'étudiants indous en Europe conservent, partiellement tout au moins, leurs coutumes alimentaires et tous les sujets européens en Inde ont un régime occidental. Leur nourriture est cependant notablement plus salée qu'en Europe de façon à équilibrer la balance sodique de l'organisme. Ceci explique vraisemblablement pourquoi nos observations ne montrent dans aucun cas une stimulation de l'activité surrénale comme celle observée en expérience aigüe, avec sudation abondante et balance sodique déficitaire (Collins, 1962).

Enfin, l'ingestion de K diminue paradoxalement la potassémie de certains sujets lorsque le K plasmatique est élevé au départ. Cette observation est en accord avec de récentes expériences faites sur l'animal qui permettent de considérer le taux de K plasmatique comme un stimulus très spécifique de la sécrétion d'aldostérone (Blair *et al.*, 1962). Il en serait de même chez l'homme. Lorsque la concentration du plasma en K est élevée, toute surcharge supplémentaire en K déclencherait une sécrétion d'aldostérone suivie d'une baisse rapide de la potassémie. La valeur de ce taux limite serait différente en pays tropical et tempéré.

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ASSESSMENT OF MODERATE THERMAL STRESS IN NATURALLY ACCLIMATIZED INDIVIDUALS

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Abstract — Native, young male Thai students were first exposed to a temperature of 45° C at 65 per cent R.H. for 1 hr. After recovering for 1 hr at 31.5° C and 63 per cent R.H. they went back to the hot room where they performed the step test (50 steps/min) and then sat down for the rest of the hour. With or without work all the subjects suffered considerably in the heat. The pulse rate rose from 80 to 98 or 106 beats/min; the blood pressure showed little change. Of the 5 psychological tests one gave better results in the heat.

Zusammenfassung — Einheimische, junge, männliche, thailandische Studenten wurden eine Stunde lang einer Temperatur von 45° C bei 65% R.F. exponiert, konnten sich danach eine Stunde bei 31,5° C und 63% R.F. erholen, ehe sie zum zweiten Mal in den heissen Raum gingen, wo sie kurz Arbeit leisteten (50 Stufen/Min), dann den Rest der Stunde ruhig sassen. Mit und ohne Arbeit litten die Personen erheblich unter der Hitze. Die Pulszahl stieg von 80 auf 98 bzw. 106/Min, der Blutdruck war kaum verändert. Bei einem von 5 psychologischen Testen wurden in der Hitze bessere Ergebnisse erhalten als im Normalraum.

Résumé — Des étudiants thailandais tous de jeunes hommes, furent exposés durant une heure à une température de 45° C par une humidité relative de 65 pour cent. Ils se sont ensuite reposé une heure durant par 31,5° C et 63 pour cent d'humidité relative. Après, ils ont de nouveau pénétré dans la pièce chaude pour y accomplir un bref travail (50 marches en 1 min) et rester assis ensuite pendant une heure. Tous souffrirent très nettement du chaud et cela avec ou sans travail. Le nombre des pulsations a augmenté de 80 à 98, respectivement 106 par minute, alors que la pression sanguine restait presque inchangée. Une parmi cinq épreuves psychologiques donna de meilleurs résultats dans la pièce chaude que dans celle présentant une température normale.

With moderate muscular activity in the absence of extreme degrees of heat and humidity pronounced thermal stress is of rare occurrence among individuals who are naturally acclimatized to a humid tropical country such as natives of Thailand. On the other hand, mild cases of incapacity due to heat are frequently encountered. We, therefore, think that a simple but sensitive index to detect impending failure of accomodation would be of value. The present experiment was performed in order to assess the value of the common tests for detecting thermal stress in the early stages.

MATERIALS AND METHODS

Two groups each of five clinically healthy male medical students, aged 21 to 24, were submitted to the following four 60-min periods of experimentation:

(1) Control period. The subjects sat at ease in comfortable chairs in a "standard room" with an air temperature of 31.5° C, 63 per cent relative humidity, and no air movement. Pulse rate and arterial blood pressure were taken at 15-min intervals and a number of psychological tests were performed between the 31st and 55th min.

(2) Inactive "heat period". The subjects moved into a climatic chamber with a temperature of 45° C, 65 per cent relative humidity and a wind velocity of 22 m/min. They remained inactive, and measurements and tests were made as in the control period.

(3) Rest period. The subjects went back into the "standard room" and sat out the period comfortably.

(4) Active "heat period". The subjects moved into the hot chamber again where they performed the step-test, 50 steps in 1 min, then sat down for the rest of the period while tests and measurements were continued.

The two groups were subjected to the same procedures with the difference that one group had the inactive heat period before the active one, while the other group had the active heat period first.

The subjects wore trousers with under-pants, a short-sleeved shirt with armless singlets, and socks and shoes. Pulse rate and blood pressure were taken in the standing as well as sitting position. The psychological tests were as follows: selection of letters of the alphabet, selection of certain numbers, recognition of specified objects, sorting of cards, judgement of subjective values, and mathematical multiplication. In each case, maximum performance in a limited time was required, and a simple, arbitrary scoring was used to give numerical values.

RESULTS AND DISCUSSION

All subjects suffered considerably from the heat while in the hot chamber, even when inactive. With exercise the heat load was reported as "hardly bearable" in a few cases. There was no instance of prostration, although recovery from the effects of exercise took an unusually long time. The two groups showed essentially similar results: therefore, the data were pooled for evaluation (Table 1). The values for pulse rate and blood pressure are the means of all measurements made during each period for each subject.

It is seen that pulse rate was the most sensitive indicator of stress in all cases, showing a distinct and marked rise even when the heat load was relatively small, i.e. with inactivity in the hot room. With additional heat production by muscular exercise the pulse rate was even higher. Contrary to expectation the arterial blood pressure had little value in this connection, exhibiting a significant change only under the condition of additional activity. When sitting quietly in the hot room, most of the subjects had a lower systolic blood pressure than when they were outside. This was especially true of measurements in the standing position. The finding was probably associated with a condition of "poor vascular tone" which prevails in many Thai subjects, and which was certainly enhanced by the hot environment. Immediately after exercise in the hot chamber the systolic pressure rose steeply, then declined rather quickly to near-normal levels, so that the mean value for the 60-min period was only a little higher than the control.

Table 1

Periods	Pulse rate		Systolic pressure		Diastolic pressure		Psychological tests				
	Sitting	Standing	Sitting	Standing	Sitting	Standing	Letter selection	Number selection	Recognition	Card sorting	Judging values
Control	78.9	78.1	92.9	89.8	58.6	59.3	91.5	138.5	96.6	43.8	13.5
Heat, inactive	98.0	106.6	93.4	89.4	60.2	67.5	92.6	184.5	96.4	44.5	15.5
Heat, active	106.3	119.3	102.5	106.6	65.4	62.1	86.3	125.5	96.6	40.0	16.5

Psychological tests were performed in the hope that they might be more sensitive than the circulatory responses, but here again the results did not meet expectation. In fact, in one instance the reverse was encountered, viz. in the heated room without exercise a few tests gave a better score than the control. This may be explained on the grounds that "moderate heat" constituted a source of irritation which stimulated rather than depressed activity; stronger heat, i.e. with an additional load from exercise, caused an impairment of efficiency which was appreciable in most tests. Another probable factor was the short duration of each test which, therefore, might not cause real psychological stress. It is possible that some other test or tests might be more suitable and more sensitive as indicators of heat stress than the ones we employed, although it is unlikely that such tests would be of practical value in assessing moderate degrees of thermal effects, especially in acclimatized persons.

DERMAL STIMULATION IN THERMAL SWEATING

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Abstract — In acclimatized subjects hot air (45° C) was applied selectively to (1) the body with exclusion of the head and neck, (2) the face, and (3) the chest in an area equal to that of the face. Sweat was absorbed on filter paper at six points during 90 min; its weight and sodium and potassium contents were fractionally determined. On application of heat to the body in men the back produced the largest quantity of sweat, and the forearm more than the thigh; in women the quantities on the forearm and the thigh were practically equal. The concentrations of sodium and of potassium remained almost constant throughout the experiment in men but there was a gradual decrease in women. When the face was heated, perspiration was smaller in quantity; application of heat to the chest diminished sweat production even more.

Zusammenfassung — Bei akklimatisierten Versuchspersonen wurde heisse Luft (45° C) wahlweise angebracht auf (1) den Körper unter Ausschluss von Kopf und Nacken, (2) das Gesicht, und (3) die Brust bei gleicher Fläche wie der des Gesichtes. Der Schweiss wurde auf Filterpapier an 6 Stellen 90 Minuten lang absorbiert; das Gewicht sowie der Gehalt an Natrium und an Kalium wurden fraktionsweise bestimmt. Bei Applikation der Wärme auf den Körper von Männern gab der Rücken die grösste Menge Schweiss ab, der Unterarm mehr als der Schenkel; bei den Frauen waren die Mengen am Unterarm und am Schenkel praktisch gleich. Die Konzentrationen an Natrium und an Kalium blieben während des ganzen Versuches bei den Männern fast unverändert. Wenn das Gesicht erwärmt wurde, war Schweissabgabe nur gering; beim Erwärmen der Brust war sie noch geringer.

Résumé — On a appliqué de l'air chaud (à 45° C) à des sujets bien acclimatés (1) à la surface du corps à l'exclusive de la tête, (2) au visage et (3) à la poitrine sur une surface égale à celle du visage. La sueur provoquée est absorbée au moyen de papier-filtre à 6 endroits pendant 90 minutes pour determiner le poids et la concentration en sodium et en potassium. Chez les hommes, l'application de la chaleur au corps produit une quantité de sueur maximum au dos et plus à l'avant-bras qu'à la cuisse. Chez les femmes, la quantité de sueur de l'avant-bras est pratiquement égale à celle de la cuisse. Les concentrations de sodium et de potassium restent constantes pendant toute l'épreuvre chez les hommes, mais baissent graduellement chez les femmes. Lorsque le visage est chauffé, la transpiration diminue en quantité. L'application de chaleur à la poitrine accentue cette diminution.

INTRODUCTION

For people living in tropical regions sweating is of prime importance. Most previous experiments on the mechanism by which heat causes perspiration has been performed on unacclimatized or acclimatizing persons (Kuno, 1956; Hellon *et al.*, 1956; Glaser and Newling, 1957; Rawson and Rendall, 1961). In this paper results are reported of experiments which were carried out with fully acclimatized subjects.

MATERIALS AND METHODS

A number of Thai subjects were exposed to a gentle air stream at a constant temperature and with only slight variations of humidity. Sweat was collected from different parts of the body to determine the weight and sodium and potassium contents. A special "sweat box" was used in which electrically heated air was directed by a slow-moving fan upon the subject: (1) on the front of the body from the base of the neck downwards, with exclusion of the face and neck; (2) on the face and neck; (3) on the middle part of the chest in an area approximately equal to that of the face and neck. The almost nude subject sat comfortably on a seat with a small backrest, and the parts of the body not being warmed were exposed to still air in the room at temperatures varying between 28° and 30° C. The velocity of the stream of heated air was less than 1 m/sec. The total volume of the box was approximately 2.3 m^3; of this 0.7 m^3 was contained in a collapsible side-extension so that at the beginning of each experiment, on opening a swinging door it could be pushed quickly inward to force heated air upon the subject, thus producing sudden warming at the desired temperatures. Thermometers placed in the box in front of and behind the subject recorded the air temperature. In all experiments this was maintained at $45 \pm 1°$ C, while the relative humidity varied from 40 to 50 per cent. Sweat was collected at 6 predetermined regions by being absorbed on a number of 5×10 cm strips of filter paper which were covered by a 2.5 cm thick foam-sponge enclosed in a plastic bag, stiffened with a thin sheet of copper bent to fit the part of the body and kept in place by a 2.5 cm wide rubber strap. Great care was taken to keep the filter paper in intimate contact with the skin without interfering with the blood circulation. Each strip of filter paper was weighed in a tared bottle on an automatic balance just before being put in place and directly after removal, and was then extracted with 50 ml of distilled water for the determination of sodium and potassium content by flame photometry.

Twenty male and 5 female medical students and 3 male and 1 female janitors were investigated. In the males collection of sweat was made on the forehead, left side of the chest, left forearm, left thigh, left infrascapular region, and left inguinal region; in females collection was omitted on the chest and groin. Each collection was made during a period of 15 min, counting from the moment the thermometers showed the correct temperature. It was repeated 6 times so that each experiment lasted 90 min. Determinations were made separately for each 15-min period.

RESULTS AND DISCUSSION

The weight of sweat absorbed at each region varied between 0.3 and 0.6 g/50 cm^2 and the concentrations of sodium and potassium varied between 100 and 220 mEq/l, and 20 and 50 mEq/l, respectively. There were fairly wide variations in the data for different subjects.

In the first series of experiments with the "body" heated, the weight of sweat collected in the males was greatest on the back, followed by that on the chest, forehead, forearm, thigh and groin. In female subjects the same quantitative order was found, with the exception that the forearm and the thigh yielded practically equal amounts (Table 1). In fact, in the female the leg appeared to perspire considerably more than in the male. This is perhaps the result of adaptation to the style of clothing.

Table 1. Total Amount of Sweat during 90 min.

	Fore-arm	Thigh	Back	Fore-head	Ingui-nal	Chest
Women "Body" heated (Mean of 6 subjects)	1483.6	1243.6	2968.8	1856.9	—	—
Men "Body" heated (Mean of 8 subjects)	1221.9	764.5	3990.2	1720.2	375.4	2218.8
Men "Face" heated (Mean of 10 subjects)	400.4	—	982.7	1248.2	248.2	500.7
Men "Chest" heated (Mean of 5 subjects)	53.2	124.6	412.9	230.98	—	—

In general, a larger volume of sweat was associated with a lower concentration of sodium and potassium. In the males these ions appeared to remain more or less uniform in concentration throughout the experiment, whereas in the females they seemed to become steadily less concentrated as time went on.

In the second series of experiments, with the "face" as the site of warming, the amount of sweat was smaller than in the first experiments in practically all sites, the difference varying from one-half to two-thirds. Sodium and potassium concentrations were little altered Theoretically speaking, the lower rate of secretion may be due to the "face" being a less sensitive region for stimulation than the "body", or to the fact that a smaller area of skin was being stimulated. The data showed clearly that when an equal area of skin on the chest was warmed, the amounts of sweat collected were as small as one-half to one-eighth of those obtained when the "face" was heated. Because of the small volume of perspiration collected its composition could not be analysed in several cases. These experiments showed that the area of surface stimulated was not the sole quantitative factor in sweating.

On the other hand, warming the "face" produced two-thirds to one-fourth as much secretion as that produced when the "body" was heated. Assuming that the "face" has a surface area of about 9 per cent that of the whole body stimulation of the "face" was producing 2 to 5 times more sweat than other parts. We think that this finding may be due to the following: (1) thermal receptors in the "face" are more effective than those in other parts of the body; (2) warming the face produces a stronger psychic stimulation; (3) blood supplying the brain is more heated when the "face" is warmed; and (4) internal heating from inspiration of hot air is acting as an additional stimulus.

ACKNOWLEDGEMENTS

We wish to express our deep appreciation of the gallant way in which our subjects co-operated in carrying out these experiments.

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CLIMATE AND RHEUMATIC DISEASES

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Abtract – The influence of climate on the prevalence of rheumatic complaints is considered from two separate points of view. Differences in macro-climate have been shown to be associated with variation in the prevalence of rheumatic fever and rheumatic heart disease. This is related to the prevalence of scarlet fever and other streptococcal infections and is explained by the sensitivity of this organism to light. Clinical rheumatoid arthritis, on the other hand, has shown much the same prevalences in two populations living in a temperate and a subtropical climate respectively. In females the disease was less severe in the sub-tropical population sample and this was associated with a lower titre distribution of rheumatoid serum factor in this group. Differences in micro-climate have been shown to influence rheumatic complaints associated with osteoarthrosis and disc degeneration but not the frequency or severity of the radiological changes.

Zuammenfa ung – Der Einfluß des Klimas beim Auftreten von rheumatischen Beschwerden wird von zwei getrennten Gesichtspunkten her betrachtet. Unterschiede im Makroklima zeigen eine Verbindung mit den Schwankungen im Vorkommen des rheumatischen Fiebers und rheumatischer Herzkrankheiten. Dies wird auf das Vorkommen des Scharlachs und anderer Streptokokken-Infektionen zurückgeführt und mit der Empfindlichkeit des Organismus für die Strahlung erklärt. Andererseits hat die klinische rheumatoide Arthritis dieselbe Form des Vorkommens in zwei Untersuchungsgruppen gezeigt, die in einem gemäßigten bzw. in einem subtropischen Klima leben. Bei Frauen war die Krankheit in der subtropischen Bevölkerung weniger schwer. Dies wurde mit einem niedrigeren Titer des rheumatoiden Serumfaktors in dieser Gruppe erklärt.

Résumé – L'influence du climat sur l'apparition des crises de rhumatisme est examinée ici selon deux points de vue différents. Les différences du macro-climat sont en rapport avec l'apparition de fièvres rhumatismales et d'affections cardiaques à caractère rhumatismal. On met cette constatation en relation avec l'apparition de fièvre scarlatine et d'infections par streptocoques et on l'explique par un état de sensibilité accrue de l'organisme au rayonnement. En outre, l'arthrite rhumatoïdique a montré la même forme dans deux groupes d'individus habitant les uns dans un climat tempéré, les autres dans un climat sub-tropical. La maladie était moins prononcée chez les femmes vivant en milieu sub-tropical. On l'explique par le fait qu'elles présentaient un taux inférieur du facteur rhumatoïde du sérum sanguin.

An association between climate and the rheumatic diseases has been thought to exist since classical times but until recently there has been little scientific confirmation of the views expressed by the earlier writers. Careful records of Rentschler, Vanzant and Rowntree (1929), Feige and Freund (1931), and Fox and van Breeman (1934) have confirmed an association between rheumatic complaints and changes in weather but there has been no agreement as to the climatic factor which is responsible.

It has frequently been stated that rheumatism is more frequent in temperate than in tropical climates, but there is little convincing evidence to back up this statement. The prevalence of the commoner forms of rheumatism is so closely related to age, that any conclusions which do not take age distribution into account are of little value. There is a tendency in tropical climates for populations, particularly in the towns, to have a larger proportion in the younger age groups and this greatly reduces the chances of finding the commoner forms of rheumatic disease such as osteoarthrosis, disc degeneration and rheumatoid arthritis in such populations.

RHEUMATIC FEVER

Such evidence as is available on climate in relation to the rheumatic diseases is concerned chiefly with rheumatic fever. As this occurs chiefly in young people it is less affected by the age distribution of the population. Hench in 1948 collected statistics from a number of hospitals in the United States of America. He found that in Boston which is on latitude 42°, 1.9 per cent of hospital admissions were for rheumatic fever or rheumatic heart disease whereas only 0.03 per cent of admissions in New Orleans at a latitude of 30° were for this cause. Admissions for rheumatic fever were 5.8 per cent of all hospital admissions amongst children in Philadelphia at latitude 39° but only 0.7 per cent in Los Angeles at 34° (Table 1). Portland,

Table 1. Hospital Admissions for Rheumatic Fever and Rheumatic Heart Disease in Children in the U.S.A. (Hench et al., 1948)

Locality	Latitude	Isotherms		Admissions for rheumatic fever as per cent of total admissions	
		Jan.	July	Children	All ages
Boston	42°	24°	65°		1.9
Philadelphia	39°	32°	74°	5.8	
Portland, Oregon	45°	40°	64°	3.5	
Cincinnati	39°	32°	76°	2.7	
Dallas	32°	48	84°	0.8	
Galveston, Texas	29°	53°	86°		0.2
Los Angeles	34°	53°	72°	0.7	
New Orleans	30°	55°	84°		0.03

Oregon though further north than Philadelphia had fewer admissions from this, cause but was warmer, having a January temperature of 40° compared with 32° in Philadelphia. There is however no direct relationship between hospital admissions and either latitude or isotherms. Galveston for example, has seven times as many admissions for rheumatic fever as New Orleans, although the latitude and temperature is almost identical. This might be due to a number of extraneous factors determining the selection of cases for hospital admission. A more reliable index of prevalence is the proportion of necropsies in which rheumatic heart disease was encountered. In Boston at 42° latitude 5.5 per cent of necropsies showed evidence of this disease, compared with 3.5 per cent at Atlanta (34°), 0.9 per cent at Galveston (29°) and 0.6 per cent at New Orleans (30°) (Table 2).

Table 2. Rheumatic Heart Disease in Necropsies

Locality	Latitude	Isotherms		Prevalence of rheumatic heart disease per 100 necropsies
		Jan.	July	
Boston	42°	24°	65°	5.5
Atlanta	34°	48°	82°	3.5
Galveston, Texas	29°	53°	86°	0.9
New Orleans	30°	55°	84°	0.6

Table 3. Rheumatic Heart Disease per 100 School Children

Locality	Latitude	Isotherms		Rheumatic heart disease per 100 children
		Jan.	July	
Wyoming	45°	27°	79°	4.5
Madison, Wis.	43°	23°	72°	2.2
New Haven, Conn.	41°	30°	72°	2.5
Eureka, Calif.	41°	48°	68°	2.1
Denver, Colo.	40°	32°	82°	1.6
Redlands, Calif.	34°	48°	80°	0.4
Dublin, Ga.	32°	48°	82°	1.0
So, Arizona	32°	56°	88°	0.5
Pensacola, Fla.	30°	52°	84°	0.3
Dade County, Fla.	25°	69°	82°	0.4

Statistics for rheumatic heart disease in school children also give a useful indication of morbidity since these are derived from routine examinations. A series of these have been collected by Saslow and Streitfield (1956) in the United States of America and are reproduced in Table 3. There was a close association between latitude and the prevalence of rheumatic heart disease. There was no correlation with the July isotherm which varies little between Wyoming at 45° and Dade County at 25° latitude. The January isotherm showed an inverse relationship but this was, on the whole, a less satisfactory fit than latitude. Climate, however, is not the only environmental factor of importance. Rheumatic heart disease is more frequent in urban than rural children and in the poorer urban districts than in the well-to-do (Paul *et al.* 1934).

Table 4. Incidence of Scarlet Fever and Rheumatic Fever in U. S. Naval Stations in 1945

Locality	Latitude	Scarlet Fever Rate/1000	Rheumatic Fever Rate/1000
Great Lakes, Ill.	42°	149	19
Sampson, N.Y.	42°	111	17
Bainbridge, M.D.	39°	80	19
San Diego, Calif.	32°	28	4
Paris Island, S.C.	34°	1.4	0.6

An important indication of the factors concerned is that the distribution of rheumatic fever has been found to be similar to that of scarlet fever, tonsillitis and pharyngitis (Table 4 Coburn and Young, 1949). The highest incidence of both rheumatic fever and streptococcal throat infections in the United States Navy

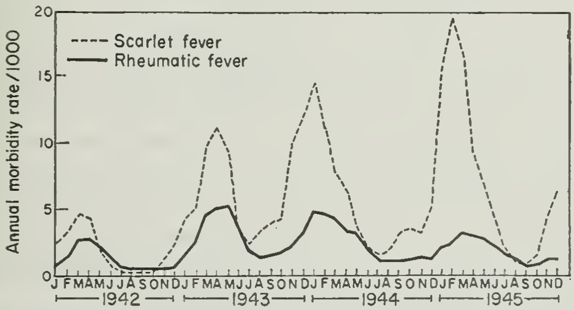

Fig. 1. Seasonal Trend of Scarlet Fever and Rheumatic Fever among Navy Personnel (from Coburn and Young, 1949)

Training Centres, during the war occurred in the Northern States. When streptococcal outbreaks took place in the south, however, they were followed by a high incidence of rheumatic fever just as in the north. The peak incidence of rheumatic fever followed that of scarlet fever by not more than a month usually between January and April (Fig. 1).

Both the geographical and seasonal incidence of streptococcal infection may be explained on the grounds that the survival of the streptococcus is diminished by exposure to warmth and sunshine. Examination of floor and blanket dust cultures by Coburn and Young (1949), for example, showed disappearance of the organism during the middle of the summer. At other times of the year the organism survived for 8 months even in a locked room. Streptococci survived for longer in Northern than in Southern Stations and there was a close relationship between the geographical location of a centre and the viability of the haemolytic streptococcus in reservoirs of dust and in blankets.

These important studies by Coburn and Young (1949) on the incidence of streptococcal infection and its causative significance in rheumatic fever have proved of great practical importance. Therapeutic trials of prophylaxis by antistreptococcal agents such as the sulphonamides and penicillin have confirmed the importance of the streptococcus (Kuttner and Reyersbach, 1943; Rubbo *et al.*, 1949). It has been found possible by administering these agents during the winter months to reduce greatly the frequency of attacks of rheumatic fever in susceptible individuals and this disease has now ceased to be an important cause of heart disease in temperate climates.

RHEUMATOID ARHRITIS

This disease is in some ways similar to rheumatic fever though it runs a more chronic course. Acute forms of polyarthritis, indistinguishable from rheumatic fever may on follow-up develop the chronic form known as rheumatoid arthritis. Though rheumatoid arthritis is said to be less common in tropical climates, the greater prevalence of the disease in the older age groups would make it unlikely that the disease would be as frequent in such populations even if a climatic effect was absent. In a comparison of two populations in which random samples aged 35 to 64 were examined, one in the north of England at latitude 54° N, the other in Jamaica at 18° N no significant difference in prevalence was observed in the females at any age though disease was less severe in the Jamaican females. In the Jamaican males there was actually a higher prevalence than in their English counterpart but only in the 55 to 64 age group and limited to those of minimal severity (grade 2). Thus it is clear that rheumatoid arthritis, though it may be less severe in a subtropical population, is not less frequent.

A characteristic feature of rheumatoid arthritis in temperate climates is the presence in the serum of macroglobulins which agglutinate rabbit or alter human γ-globulin. These macroglobulins are present in high titre in some 80 per cent of patients with arthritis but in only 2–5 per cent of individuals in random population samples. When they are present in a patient with arthritis, the joint disease is usually severe and persistent. A number of tests for these macroglobulins are available. The sheep-cell agglutination test which uses rabbit globulin was positive at a titre of 1 in 32 in 2.4 per cent of the Jamaican males (Table 6). This is only

Table 5. Prevalence of Clinical Rheumatoid Arthritis in Random Population-Samples in Jamaica and in the North of England

Males	Grade of Clinical Rheumatoid Arthritis																
	Jamaica								North of England								
Age	Total	0	1	2	3	4	2–4 per cent	3–4 per cent	Total	0	1	2	3	4	2–4 per cent	3–4 per cent
35–44	89	82	6	1	—	—	1	0	185	169	12	4	0	0	2	0
–54	87	79	7	1	—	—	1	0	235	207	19	6	3	0	4	1
–64	87	70	6	8	3	—	13	3	143	131	7	2	2	1	3	2
Total	263	231	19	10	3	—	5	1	563	507	38	12	5	1	3	1
Females																
35–44	91	78	6	5	1	0	7	1	214	180	24	9	0	1	5	0.5
–54	89	77	5	7	0	0	8	0	227	177	37	11	2	0	6	1
–64	91	73	7	9	2	0	12	2	179	136	24	12	4	3	11	4
Total	271	228	18	21	3	0	9	1	620	493	85	32	6	4	7	2

Table 6. Rheumatoid Serum Factors in Random Population Samples in Jamaica and in the North of England

Age *Males*	Sheep cell Agglutination titre												
	Jamaica									North of England			
										Urban + Rural		Rural only	
	Total	< 4	4	8	16	32	64	128	256	32+	Expected	32+	Expected	32+
35–44	84	79	3	1	1	—	—	—	—	0%	1.8	2%	2.0	2%
–54	83	72	8	–	–	1	1	1	—	4%	3.5	4%	0.9	1%
–64	82	73	4	2	–	2	—	—	1	4%	2.3	3%	0	0%
Total	249	224	15	3	1	3	1	1	1	2.4%	7.6	3.0%	2.9	1.1%
Females													
35–44	83	72	7	3	1	0	0	—	—	0%	1.8	2%	0.9	1%
–54	83	73	7	2	1	0	0	—	—	0%	4.4	5%	3.1	4%
–64	85	76	6	0	1	1	1	—	—	2%	3.1	4%	4.1	5%
Total	251	221	20	5	3	1	1	—	—	0.8%	9.3	3.7%	8.1	3.2%

slightly less than the proportion of 3.0 per cent which would be expected in a sample of males of the same age distribution in the north of England. As however the titre is higher in urban than rural populations comparison should preferably be made with a rural population in England. When this was done it was found that the proportion of positive tests was, if anything, rather higher in the Jamaicans. Of the Jamaican females only two had a positive test, a proportion of 0.8 per cent whereas 3.7 per cent would be expected from the surveys in northern England and 3.2 per cent if only the rural sample is considered ($P \simeq 0.03$). The reason for the low sheep-cell titre in females is not clear but may explain the comparatively mild arthritis found in Jamaican females.

It is known from animal experiments that a positive sheep-cell test results from repeated inoculation of bacteria such as *S. agalactiae*, *Str. moniliformis* and *E. coli* into rats and other experimental animals (Svartz, 1961; Lerner *et al.*, 1960; Abruzzo and Christian, 1961). No doubt other micro-organisms are capable of stimulating this response. The differences found between females in Jamaica and England should prove a useful clue to the factors responsible for the appearance of these macroglobulins in the serum.

DEGENERATIVE JOINT DISEASE

There is as yet no indication of any regional differences in the prevalence of degenerative types of rheumatism such as disc degeneration and osteoarthrosis. There is however some information on the influence of wet conditions. In a survey of rheumatic disease in the town of Leigh in north-west England (Kellgren *et al.*, 1953) the population sample included many coalminers and outdoor workers, whose occupation exposed them to wet working conditions. When those working in dry and wet conditions were compared (Fig. 2) it was found that rheumatoid arthritis recurred in much the same proportion in dry and wet work. Osteoarthrosis on the other hand, was diagnosed twice as often in wet as in dry workers and intervertebral disc degeneration four times as often in the wet workers. These data are based on clinical diagnoses and thus refer to persons with rheumatic complaints. Asymptomatic forms are thus excluded. After the survey in Leigh a list of houses classified as damp, was obtained from the Council inspector. When a comparison was made of the prevalence of rheumatic complaints in these damp houses and in the remainder, it was found that rheumatoid arthritis was diagnosed just as often amongst those living in the wet houses as in the dry, but that a diagnosis of osteoarthrosis or of disc degeneration was more commonly made in the occupants of wet houses (Fig. 3). Other forms of rheumatism such as spondylitis, gout, bursitis and synovitis did not show this relationship to damp.

To investigate this further, coal-miners working in wet and dry seams were compared. In addition to a clinical examination they were submitted to routine X-rays of a number of joints including the lumbar spine and knees. Information was thus available on both symptomatic and asymptomatic form. The miners were divided into 3 groups: (1) Those who had never worked in wet, (2) those who had worked for less than 5 years and, (3) those who had worked more than 5 years in a wet seam (Fig. 4). There was a clear relationship between back-hip-sciatic pain and damp. With increasing work in wet the number with no pain became less and the number with incapacitating pain increased. The proportion with severe disc degeneration, as determined by the X-rays, on the other hand was unaltered and of those with multiple disc involvement was the same in the "wet" and "dry" miners. The effect of wet conditions therefore is not to increase the amount of disease but to bring out the symptoms, to convert the disease from a dormant symptomless state into a painful disabling condition. Similarly osteoarthrosis of the knees was found to be more often associated with pain and loss of work in those miners who worked in the wet seam though the severity of the X-ray changes was not increased. This effect is made possible by the fact that disc degeneration and osteoarthrosis are normally asymptomatic. Osteoarthrosis for example, is symptom-free in some 75 per cent of cases.

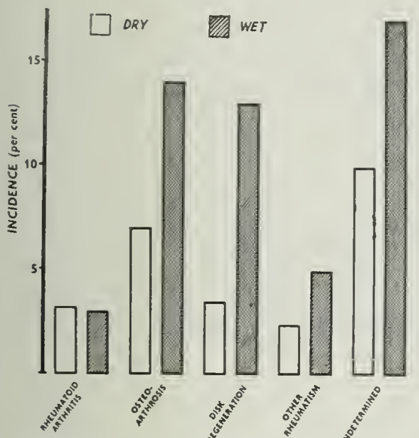

Fig. 2. Rheumatic complaints in dry and wet working conditions

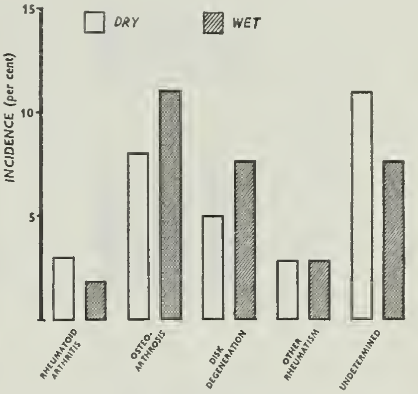

Fig. 3. Rheumatic complaints in dry and wet houses

It would appear that damp produces this effect by impairing the insulating quality of the clothing and so enabling cooling of the superficial tissues to take place. It is known from the work of Kellgren, McGowan and Hughes (1948) that the threshold to deep pain depends on the temperature of the tissues at the site of the pain. Appreciable cooling of these tissues occurs on exposure to cold or damp just as the opposite effect is produced when these painful conditions are relieved by treatment with short wave diathermy which raises the temperature of both superficial and deep tissues.

This is supported by the finding of Tromp (1963) that rheumatic patients more often complained at times of falling temperatures, strong winds, the passage of cold fronts and the influx of polar air masses. This influence was more striking in males. There was a gradual decrease in the monthly average of complaints from January to May followed by an increase.

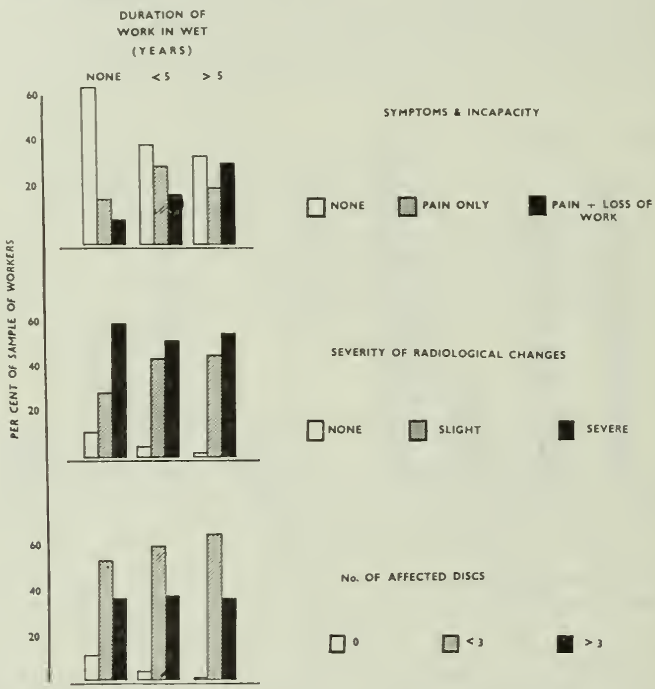

Fig. 4. The Relation of spinal symptoms and radiological changes to work in wet

ACKNOWLEDGEMENT

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ASPECTS MÉDICAUX DE LA BIOMÉTÉOROLOGIE NAVALE

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Abstract – During recent years we have studied some medical aspects of nautical biometeorology with particular reference to the behaviour of acute morbidity during ship's courses crossing very different climates. According to our findings the influence of climate on morbidity seems to be due to different factors such as variation of the seasons between departure and arrival, disturbance of nictemeral rhythms, sudden change of climatic factors such as temperature, atmospheric pressure, relative humidity and in particular the crossing of meteorological fronts. Rheumatic diseases seem to be significantly correlated with low temperature, relative humidity and high barometric pressure. Low barometric pressure seems to have an influence on the acute circulatory diseases. The influence of the climatic variations was also considered in relation to pre-existing diseases. Subjects with constitutional asthenia, neuro-endocrine instability, heart disease, liver disease, asthma and diabetes seem to be particularly sensitive to the nautical meteorological influences.

Zusammenfassung – Während der letzten Jahre haben wir einige medizinische Fragen der nautischen Biometeorologie untersucht, besonders bzgl. der akuten Sterblichkeit auf Schiffsfahrten, die durch sehr unterschiedliche Klimate hindurchführten. Wir fanden, daß der Einfluß des Klimas auf die Sterblichkeit von verschiedenen Faktoren abzuhängen scheint wie vom Jahreszeitenwechsel zwischen Abfahrt und Ankunft, der Störung des Licht-Dunkel-Rhythmus, von der plötzlichen Änderung der klimatischen Faktoren wie Temperatur, Luftdruck, relative Feuchte und besonders vom Durchfahren meteorologischer Fronten. Rheumatische Erkrankungen scheinen überzufällig von tiefer Temperatur, relativer Feuchte und hohem Luftdruck abhängig zu sein. Der Einfluß tiefen Luftdrucks scheint für akute Kreislaufkrankheiten Bedeutung zu haben. Ferner wurde der Einfluß klimatischer Änderungen auf schon vorhandene Krankheiten untersucht. Die Versuchspersonen mit konstitutionell bedingter Asthenie, neuro-endokriner Labilität, Herzkrankheiten, Lebererkrankungen, Asthma und Diabetes schienen gegenüber meteorologischen Einflüssen während einer Seefahrt besonders empfindlich zu sein.

Résumé – Au cours de ces dernières années, on a étudié différents aspects médicaux de la biométéorologie nautique en se basant tout particulièrement sur l'apparition d'affections aigües au cours de croisières traversant des zones aux climats très différents. En accord avec les résultats obtenus, l'influence du climat semble se rapporter à différents facteurs météorologiques tels que changements de saisons entre le départ et l'arrivée, déréglement du rythme nycthéméral, variations brusques de la température, de la pression atmosphérique et de l'humidité relative ainsi que – et surtout – le franchissement de fronts météorologiques. L'activation d'affections rhumatismales semble être en corrélation significative avec de basses températures, une faible humidité relative et de hautes pressions atmosphériques. L'influence de basses pressions semble se faire sentir principalement dans les affections aigües du système circulatoire.

L'influence des variations du climat a également été considérée en relation avec des maladies préexistantes. Les sujets atteints d'asthénie constitutionnelle, d'instabilité neuro-endocrine, de faiblesse cardiaque, dē maladies du foie, d'asthme et de diabète ainsi que les femmes ayant une instabilité du métabolisme des graisses semblent particulièrement sensibles aux influences météorologiques nautiques.

La biométéorologie navale est l'étude de plusieurs problèmes qui concernent l'activité de l'homme sur la mer, et cela dans le cadre de la biométéorologie.

De nombreux auteurs on déjà précisé l'action du climat maritime, particulièrement en ce qui concerne son application thérapeutique.

La biométéorologie navale s'occupe des modifications biologiques qui interviennent dans l'organisme exposé au climat marin. Mais elle étudie surtout les effets biologiques des variations météorologiques qui concernent la navigation.

On sait que les objets des études biométéorologiques sont les réactions biologiques déterminées par les variations du climat.

Ces réactions, pour ce qui se rapporte à l'homme, peuvent se présenter sous la forme de modifications lentes et fonctionelles de l'organisme. Celui-ci doit s'adapter aux variations du climat et rendre sa défense plus efficace contre les agents pathogènes. Il doit cependant se maintenir dans un état toujours équilibré et faire preuve d'économie de ses forces. Quelques fois, ses réactions sont plus rapides et plus violentes et elles présentent un aspect franchement dynamique en déterminant des modifications immédiates, par exemple de nature circulatoire, respiratoire, neuro-végétative ou du métabolisme général.

Dans notre cas, nous avons pour objet d'observation des hommes qui naviguent à bord de bateaux. Ceux-ci se déplacent plus rapidement que par le passé, passent très souvent d'un climat à un autre, climats très différents les uns des autres. Les hommes qui les montent se trouvent ainsi dans la nécessité de s'adapter rapidement. Cela implique naturellement plusieurs problèmes délicats et difficiles à résoudre.

On ne doit pas oublier que les rythmes biologiques reliés aux rythmes soit saisonniers soit nycthéméraux sont également perturbés. En effet, dans les climats tempérés, le corps humain s'adapte à une succession rythmique des saisons chaude et froide séparées par des saisons intermédiaires durant lesquelles on constate des phénomènes périodiques d'adaptation. Dans le cas du déplacement rapide d'un bateau, on peut être obligé de s'adapter rapidement à des conditions climatiques défavorables et inconstantes. L'organisme peut·également se trouver dans la nécessité de modifier ses activités rythmiques, activités auquelles on accorde aujourd'hui de nouveau beaucoup d'importance.

La biométéorologie navale semble avoir pour cela des caractéristiques propres représentées surtout par une conception plus dynamique de l'action du climat qui, en obligeant l'organisme à s'adapter rapidement, engendre des phénomènes de déséquilibre et de stress qui, intervenant ensemble, peuvent souvent conduire à des états pathologiques. Le contact entre la biométéorologie navale et la physiopathologie clinique devient, de ce fait, naturel et immédiat.

Ces dernières années, notre Institut a étudié les aspects médicaux de la biométéorologie navale en vouant une attention particulière aux routes maritimes qui emmènent l'homme dans les zones tropicales et équatoriale.

En effet, les modifications météorologiques et les zones de discontinuité que le bateau rencontre pendant ses déplacements rapides le long des méridiens, représentent les conditions extrêmes d'un conflit entre la vie et le climat.

Au cours de ces voyages, l'homme rencontre et traverse de véritables fronts météorologiques caractérisés par des variations sensibles de la pression, de la température, de l'humidité et du champ électrique.

Ces routes sont celles qui concernent plus spécialement le trafic maritime de l'Italie et qui nous ont posé les plus graves problèmes du point de vue de la pathologie et de la médecine du travail.

Pour caractériser les réponses de l'organisme aux agressions auxquelles il est soumis pendant un long voyage en mer comprenant la traversée des tropiques, on a mis en évidence une série de phénomènes qui peuvent être la cause d'événements morbides très bien corrélés.

L'altération évidente des conditions hémodynamiques semble avoir une importance considérable dans la pathogénèse des événements morbides endommageant le système cardio-circulatoire.

Un sujet brusquement exposé à l'action du climat tropico-équatorial voit sa température cutanée se relever sous l'action de la hausse de la température ambiante. Le gradient température centrale — température cutanée s'en trouve réduit, ce qui entraîne une hausse de la température du sang veineux et une stimulation des centres vasomoteurs. Il s'ensuit une intense vasodilatation périphérique accompagnée d'hypotension systolique et diastolique ainsi que de troubles circulatoires qui peuvent quelques fois se révéler très sérieux.

Dans un climat tropico-équatorial, la déperdition calorique n'est pratiquement causée que par la transpiration. Il s'agit, comme on le sait, d'un processus conditionné d'un côté par l'activité des glandes sudoripares et de l'autre par la rapidité d'évaporation de la sueur produite.

On a constaté que la transpiration et la perte d'eau qui en résulte sont plus élevées chez les sujets les moins adaptés parmi les membres d'un équipage et encore plus parmi les passagers. On remarquera en outre que, dans ces conditions, la sueur est plus riche en ions Na et K dont la perte est donc plus importante.

Dans ces conditions, les quantités de liquides ingérés augmentent jusqu'à atteindre des doses journalières très élevées, surtout dans des conditions particulièrement défavorables (par exemple dans les salles de chaudières et de machines des bateaux navigant sur la Mer Rouge ou le Golfe Persique).

La diminution de la masse sanguine résultant de l'abondante perte hydrique, diminution qui n'est souvent pas compensée intégralement par des ingestions d'eau, détermine également des répercussions dans le système circulatoire.

Dans ces conditions, l'oligurie, l'hypoclorurie et l'hyponatrurie demeurent constantes, tandis qu'augmentent les pertes en potassium.

Chez les sujets exécutant des travaux pénibles, les essais de diurèse provoquée, donnent des résultats insuffisants.

L'oligurie semble conditionnée à une diminution de la filtration glomérulaire par suite de la diminution de la masse du sang.

La vasodilatation périphérique et la diminution de la masse du sang contribuent toutes deux à causer d'importantes modifications circulatoires, signalées tout d'abord par une diminution plus ou moins accentuée de la pression artérielle.

Lors du passage du climat tempéré nordique au climat tropico-équatorial marin, on a constaté un comportement constant et univoque de la pression sanguine. Celle-ci diminue — plus spécialement la pression sistolique — mais ne comporte pas de différences sensibles entre passagers et membres de l'équipage.

La pression artérielle redevient normale après que l'on ait dépassé la zone tropico-équatoriale et que l'on ait pénétré dans la zone tempérée de l'hémisphère austral. Pendant le passage de la zone tropico-équatoriale, les pulsations de la plupart des sujets sont légèrement plus rapides.

L'étude du comportement de l'appareil neuroendocrinien présente un intérêt extrême. En effet, il est bien connu que la plupart des effets biologiques du climat se réalisent par le canal du système nerveux végétatif. Ceci résulte des différentes recherches effectuées par plusieurs auteurs qui ont remarqué que, parmi des sujets exposés à l'action du climat tropico-équatorial, des déséquilibres fréquents se produisent, surtout d'ordre sympathicotonique ou vasotonique.

Dans la plupart des cas étudiés, d'Avanzo a observé une diminution du taux glycémique quelques fois sensible, qu'il admet être l'expression d'une réaction vagotonique. Il semble en effet, d'après les constations faites également par d'autres auteurs, qu'un pareil trouble neurovégétatif peut se manifester tout d'abord sous l'action d'un climat tropical.

Il est toutefois vraisemblable que ces conditions sont relatives à la constitution individuelle notamment à son composant neuro-végétatif et endocrinien.

En ce qui concerne plus strictement l'appareil endocrinien, on se souviendra des recherches faites sur le comportement du métabolisme basal, recherches qui ont généralement abouti à supposer un état d'hypoactivité de la glande thyroide.

D'autres recherches démontrent une hyperactivité surrénale. Le climat tropico-équatorial provoque une hypersécrétion de ACTH et il en résulte une stimulation des surrénales. On a vu en outre que l'administration de DOCA à des sujets qui n'étaient pas acclimatés en faciliter l'adaptation aux stress tropicaux.

On rappellera à ce propos que la perte des facultés d'adaptation, annoncée par l'hypotension, l'asthénie physique et psychique, doit être attribuée à une insuffisance cortico-surrénale.

On peut suggérer à ce moment-là de faire une comparaison entre les difficultés qu'ont certaines personnes à s'adapter rapidement à un nouveau milieu et leur manque de résistance aux maladies infectieuses.

Des recherches particulières ont été entreprises à notre Institut sur l'apparition de maladies aigües de l'équipage et des passagers pendant des voyages transocéaniques. Ces recherches ont porté surtout sur l'influence des différents éléments météorologiques.

Zannini et Tortori Donati ont comparé pendant une série de voyages transocéaniques la santé et les données géographiques et climatologiques telles que: la mer traversée, la position géographique, la saison, la température, la pression atmosphérique, l'humidité relative et la direction du vent.

L'étude des rapports existant entre les différents éléments météorologiques d'une part et les symptômes pathologiques d'autre part a montré que les maladies du système respiratoire sont plus fréquentes par de basses températures et une faible humidité relative.

Les affections rhumatismales semblent être en corrélation significative avec les différents éléments météorologiques, c'est à dire plus fréquentes par basses températures, faible humidité relative et pression barométrique élevée.

L'action de la pression atmosphérique semble avoir une importance particulière pour les maladies aigües de la circulation, puisque ces dernières se manifestent surtout par basses pressions. Il ne faut pas oublier, à ce propos, que certaines affections circulatoires se manifestent plus facilement pendant la nuit, au moment où la pression atmosphérique présente les baisses les plus évidentes et où l'organisme subit des variations fonctionnelles dans le domaine du système nerveux végétatif. Ces variations ont une importance considérable du point de vue pathologique.

Par ailleurs, Odaglia et de Carolis ont étudié 990 cas de cardiopathie chez les gens de mer afin de cristaliser les caractéristiques d'incidence et de développement de l'infarctus du myocarde. Ils ont aussi noté une action négative des variations climatiques rapides rencontrées au cours de la navigation.

Parallèlement, Fontana a étudié pendant dix ans les cas d'infarctus dans la région de Savona et il a trouvé une corrélation significative entre leur fréquence et les variations météorologiques.

On a aussi étudié l'action des variations des éléments météorologiques rencontrées au cours de la navigation sur des sujets déjà atteints de diverses maladies. On constate alors un effet pernicieux dû aux variations rapides du climat. Les cardiaques, les hépatiques, les asthmatiques, les sujets endocrinopatiques et les névropathes semblent éprouver le plus cet effet pernicieux.

RESPIRATORY AND PULSE RATE AND BLOOD PRESSURE INDICES AS PARAMETERS OF ACCLIMATIZATION IN STUDENTS

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Abstract – The purpose of the report is to show the results of investigations on the acclimatization of sportsmen to changed conditions of the climatic environment. This problem is not only of scientific importance but has also practical significance. Blood pressure, pulse rate and respiration frequency were examined and worked out according to indices of Hildebrandt and Kerdö which reflect the state of nervous strain of the vegetative system. Undergraduates of the High School of Physical Education in Poznań were subjects during these investigations (97 male and 63 female students). A total number of 834 examinations was carried out. On the basis of changes of the Hildebrandt index in the mountains the tested group showed an increase in lability of the nervous vegetative system. This nervous state lasted as long as four weeks after the return to the lowlands. The analysis of the Kerdö index showed only slight changes in the tension of the vegetative system with female students and a distinct increase of tension in the parasympathic system with male students.

INTERACTION BETWEEN HOUSING COMFORT AND SEASONAL INFLUENCES ON KETOSTEROID EXCRETION IN SOUTH INDIAN MEN

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PRELIMINARY results of a determination of 17-ketosteroids in urine of 69 undernourished workers and 36 students, 20-to 35-years old, in Southern India were presented. The results are summarized in Fig. 1. It was found that among the

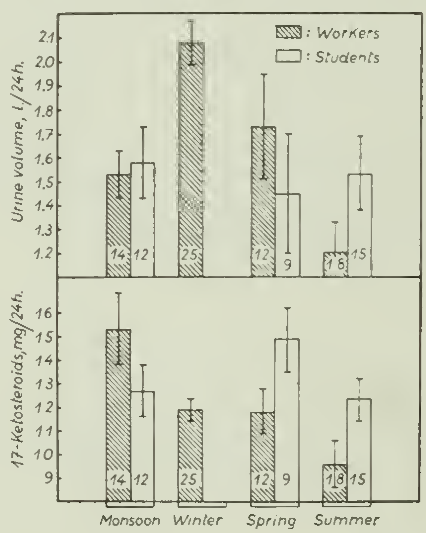

FIG. 1. Urine volume and 17-ketosteroid excretion of Indian men at various periods of the year. For each group the mean standard-error and number of subjects are given in the lower part of each column

workers the 17-KS excretion was higher in spring than in summer. The difference between the social groups is explained on the basis of the housing conditions. It is suggested that good housing conditions may lessen the influence of weather on changes of adrenal cortex activity.

STATISTICAL ANALYSIS OF VEGETATIVE REACTIONS UNDER VARIOUS METEOROLOGICAL CONDITIONS

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THE primary effect of meteorological factors on the organism is a change in the autonomic regulation. In most cases, two main types of vegetative reaction may be distinguished: an ergotropic or a trophotropic one. By means of a vegetative index used for the detection of such reactions, the author succeeded in proving statistically significant vegetative effects of various weather conditions. The results could provide a general basis for medical meteorological forecasting.

THE INFLUENCE OF METEOROLOGICAL FACTORS ON VARIATIONS OF THE pH LEVEL IN URINE

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The importance of the fluctuations of the acid-base balance in the regulating processes of the organism has been demonstrated by many investigators. Examinations were carried out to determine whether changes in the pH level of urine show a correlation with meteorological and cosmic factors. It could be established that some weather conditions have a significant influence on acid-base balance. But not all reactions could be explained by taking only meteorological factors into consideration. In special cases the cosmic influence is also significant.

TUBERCULOUS PULMONARY BLEEDINGS IN THEIR RELATION TO WEATHER AND SEASONAL VARIATIONS

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THE purpose of the present paper is to investigate the meteorotropic and seasonal influences on tuberculous pulmonary haemorrhage.

The discussion deals with cases clinically established throughout the year 1959 in the province of Poznań (central-western Poland), as recorded in 8 anti-tuberculosis therapeutic establishments with 873 beds. Altogether 85 pulmonary haemorrhages and 633 cases of haemoptysis, lasting for more than 3 days and nights, were recorded.

The weather types in Poland and central Europe were characterized according to an analysis of the weather maps (for 0:00 and 12:00 hr G.M.T.). The classification of weather conditions was based on air pressure distributions.

In the mathematical treatment of the data, the following statistical methods were applied:

(a) super-randomness index (index of meteorotropism); (b) probability calculus; (c) T-method according to Schelling and, (d) Bernoulli's dispersion formula.

The meteorobiological analysis revealed:

(1) a statistically significant correlation between pulmonary haemorrhage and "Low" in stadium of cyclogenesis—Lg; for the remaining weather situations, the values computed were found to lie below those expected and, partly, within the limits of randomness;

(2) with regard to pulmonary haemoptysis, there were no well-defined correlations with the weather types (some of the values were within the limits of randomness).

Moreover, on the basis of the data collected, an attempt was made to detect daily and seasonal rhythms of tuberculous pulmonary bleedings. The following observations were made:

(3) A maximum of haemorrhages seems to occur in a 24-hr rhythm between 12:00 and 18:00 hr.

(4) No well-defined seasonal dependence of pulmonary haemorrhage could be detected. The yearly rhythm revealed several maxima of about the same height (January, April, June, November).

(5) Pulmonary haemoptysis revealed a marked seasonal maximum (autumn and winter peak).

HIGH MAGNETIC FIELDS IN TERMINAL CANCER AND OTHER ILLNESSES

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The purpose of our study is to show that in contrast to the consensus of most scientists, at least in the U.S.A., there are profound physiological effects of high magnetic fields, e.g. in the treatment of cancer, but also in a variety of other diseases such as osteo and rheumatoid arthritis, peptic ulcers, anxiety and depression states, menopausal syndrome, bursitis and acute inflammations.

BIOSYNOPTICAL ASPECTS OF MEDICAL-METEOROLOGICAL FORECASTING

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In preparing a medical-meteorological forecast one has to take into consideration the synoptic situation of the weather. The analysis of the synoptic situation requires the most exact and the finest method in this field. According to the reactions of the human body it is necessary to distinguish two main types of weather situation, depending on the association with a warm or with a cold front passage. It is also very important to take into account the dynamic effects of the influx of various kinds of air masses in the higher level of the troposhere. Also the role of cosmic factors, chiefly the variation of the Sun's activity cannot be neglected.

THE EFFECT OF PHYSICAL EXERCISE ON THE BIOLOGICAL RHYTHM OF THE PITUITARY-ADRENAL SYSTEM

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THE excretion of uropepsin, 17-ketosteroids and creatinine in urine of young men, aged 19–26, at rest and at work (rowing training for 1 hr or skiing) was determined for different periods during 24 hr. It was found that under the influence of exercise (a) the uropepsin excretion increased before noon while at rest the uropepsin excretion decreased during this time, (b) the 17-KS excretion after exercise was lower in the morning after a day of exercise than after a day of rest (Table 1), (c) the excretion of creatinine which shows little variation in the 24-hr period increased distinctly after exercise, (d) the eosinophil count was decreased after exercise at times when it is high during the daily rhythm at rest.

Table 1

Hours (C.E.T.)	Output	17-KS average	δ	P.
07:00–13:00	at rest	19.6 mg	5.96	0.01
07:00–13:00	after exercise	13.7 mg	6.15	0.01
13:00–19:00	at rest	3.2 mg	1.88	0.1
13:00–19:00	after exercise	3.5 mg	1.17	0.4
19:00–07:00	at rest	3.0 mg	1.17	0.4
19:00–07:00	after exercise	4.6 mg	1.72	0.1

SUMMARY REPORT

D. ORDMAN

THE Specialized Working Group "Human Biometeorology" has developed from the original "Allergic Diseases" Working Group which dealt with the effects of weather and climate on allergic disorders. At the International Congress of the Society held in London in 1960 the writer suggested that it was not sufficient to have a Working Group dealing with allergic diseases alone and he proposed that the scope of this Group be extended to include human diseases in general. This proposal was accepted and from that time onwards the relative Permanent Committee has been known as the "Committee for the Study of the Biometeorological Aspects of Human Diseases" with a Sub-Committee on Allergic Diseases. This International Permanent Committee consists at present of 55 members representing 33 countries.

At the 1960 International Congress in London the Working Group on Allergic Diseases was rather poorly represented with physicians. It was then a matter for regret that so few medical men appeared to be interested in the investigations regarding the relation of meteorology to human diseases. At the present Congress in Pau in September 1963 the number of physicians had increased but it is hoped that in the future there will be a still larger representation of medical men. There is a great need for the recognition by physicians of the possible influence of weather and climate on the health and illness of their patients and as a consequence for systematic, organized scientific studies.

In an ordinary way a Congress implies the meeting of specialists in one or other discipline for close and intensive study of the particular speciality. The International Congress of Biometeorology provides something greater in that there is a gathering in conference of specialists in different biological disciplines but drawn together by a common link – the influence of weather and climate on living organisms. This type of Congress is of the very highest importance indeed because it permits of the meeting in discussion of people who have otherwise small opportunity for comparing and contrasting the findings in their different disciplines which have emerged from the investigations in their own particular highly specialized fields. So much is it possible to learn from these contacts that often one cannot but feel the need for the "integrator" of scientific disciplines in addition to the specialist confined to a particular type of investigation.

MEETINGS OF THE WORKING GROUP—"HUMAN BIOMETEOROLOGY"

The specialized Working Group – "Human Biometeorology" – was under the general chairmanship of Dr. David Ordman and consisted of 10 Sections as follows:

Section	Chairman
1. Asthma, Weather and Climate	D. Ordman
2. Bronchitis, Weather and Climate	D. Ordman
3. Common Colds and Influenza in relation to Weather and Climate	C. H. Andrewes
4. Influences of Weather and Climate on Various Diseases – Including Allergic Disorders	D. Ordman
5. Basic Physiological Mechanisms (except Thermoregulation) in relation to Weather and Climate	M.I. Halhuber
6. Clinical aspects of Thermoregulation in relation to Weather and Climate	E.M. Glaser
7. Nautical Biometeorology	F. Molfino
8. Biological effects of Aerosols	K. Dirnagl
9. Climatotherapeutic Methods	I.H. Kornbluch
10. Meteoro-pathological forecasting.	F. Sargent.

The Working Group met on five days and 38 papers were presented. Most of these papers were of a relatively high standard. Discussion was usually keen and of value but there was hardly sufficient time in many of the sessions to permit of adequate discussion. So much was this difficulty felt that a whole morning was set aside entirely for continued discussions, more especially on the subjects of the relation of meteorology to the common cold and to allergic conditions. In a sense such extra time for discussion is not desirable at Congress because this time could have been usefully spent by members of this Group anxious to attend the meetings of other Working Groups to mutual advantage.

There was evidence in the addresses and discussions of the often widely-varying outlooks of members regarding the influence of meteorological conditions on human disease. Different methods of approach to the study of human biometeorology were advanced and some difficulty was experienced by certain members because of the delivery of papers in languages with which they were not familiar. Of greater import however, is the fact that even in the papers delivered in a language understood by all, scientific phrases and expressions were often used which were ill-defined and thus not conveying the same sense to all the listeners. It became obvious that before satisfactory discussions could take place there must be standardization of medical and meteorological terms. It would seem that emphasis should be laid in circulars to prospective participants in Congress on the advisability of defining clearly the important medical and meteorological terms used in their papers.

More emphasis should be given by writers of papers in regard to the suggested mechanism of any effect climate and weather is thought to have on human disease.

The dictum by an investigator that certain diseases are more common in his region under certain climatic conditions would have a greater value if supported by an hypothesis as to the type of physical or physiological mechanism involved. Further, a clear-cut line of differentiation must be drawn between the *indirect* effects of weather, e.g. in pollen asthma, and the *direct* effects of weather and climate on persons, e.g. in possibly favouring infection, digestive disturbance, emotional factors, etc. which could assist in the precipitation of the morbid conditions under review.

NATURAL AND ACQUIRED ACCLIMATIZATION AT HIGH ALTITUDE

Chairman: W. H. Weihe

INTRODUCTION

W. H. WEIHE

A YEAR ago I had the pleasure of organizing an International Symposium on The Physiological Effects of High Altitude which was held in Interlaken, Switzerland, from 18 to 22 September, 1962 (Weihe, 1964). During the symposium it soon became evident that there is disagreement between zoologists and human physiologists about the interpretation of the terms *adaptation* and *acclimatization*. For the zoologist adaptation means genetically fixed properties developed during generations of life in a new environment while for the human physiologist it means transient changes of physiological functions during the early period of acclimatization. For the physiologist acclimatization covers all changes of body functions and is specified as *acquired acclimatization* if only transient changes leading to a new physiological equilibrium are considered, as *natural acclimatization* when the new steady state has reached an optimal value and has been maintained for generations. The latter is identical with the concept of adaptation of the zoologist. It became obvious that the human physiologist has a more differentiated view of the adaptation-acclimatization process. He sees two forms of acclimatization, natural and acquired acclimatization, the latter being subdivided into early acclimatization or adaptation, also called accommodation. In this context the interpretation of these terms given by MacFarlane in Tromp's book *Human Biometeorology* (Tromp, 1963) may be quoted:

"*Acclimatization* is the complex of reversible changes of physiological response which increase the efficiency of the individual organisms while they remain in an environment outside the neutral zone.

Adaptation has two connotations: (a) biologically it is used to generalize the concept of evolutionary adjustment of species over generations, as mutations are selected by environmental stresses, (b) physiologically adaptation connotes the rapid changes of cellular functions brought about by continued stimuli. The term applies mainly to nerves and receptors. Often adaptation is used, however, as a synonym for acclimatization."

What is high altitude? Since De Soussure reached the summit of Mont Blanc in 1789 up to the beginning of this century, high altitude has always been the biosphere within the height of mountains. Later aviation, and at the beginning of World War II, rocketeering, enabled man to travel higher and into the outer space in a capsule in which his natural biosphere is maintained. This led to an enlargement of the idea of high altitude. As the biologist sees it, high altitude is nowadays divided into lower and higher altitude ranges. The lower range of the natural biosphere, which is within the height of the mountains of the world, can be conquered without an artificial biosphere, the higher range can only be conquered, if the biospheric conditions (temperature, humidity, air pressure and air composition) of the lower range are artificially provided. The high altitude which concerns the biometeorologist primarily is the natural biosphere of the lower range.

Finally, why is high altitude physiology important for the biometeorologist? High altitude provides extreme climatic conditions. During a stay at high altitude all the adaptative functions of the body are stimulated and can be studied, so that a complete picture of the process of acclimatization can be formed. The sum total of these functions can be measured at any stage after entry into the high altitude climate. This permits the elaboration of a scheme of time sequence of acclimatization patterns to an extreme climate which can serve as a model for other biometeorological studies. Such a model can be applied for the better understanding of adaptation-acclimatization processes to less extreme meteorological and climatic changes. Slight climatic changes provide weak stimuli which are more difficult to detect and verify compared with the strong stimuli provided by extreme climates such as high altitudes.

Human biometeorologists need a complete picture of acclimatization specified for every age and racial group, for sex, state of training, mental attitude, extremity of climate and speed of change of climate. This picture permits the biometeorologist to forecast the appearance of physiological and pathological responses, to decide on suitable diagnostic tests and to recommend protective measures. In addition, this knowledge on native life or life acclimatized to high altitude can also be applied for the public health service of communities of high altitude natives and newcomers who, for various reasons, have to stay at high altitudes for long periods.

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THE STRESS OF HIGH ALTITUDE ENVIRONMENT UPON CATTLE

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Abstract – The spontaneous occurrence of congestive right heart failure (high mountain or brisket disease) in cattle at high altitudes attests to the stress of altitude adaptation within this species. Experimental cattle taken from low elevations to altitudes of 10,000 ft and above develop moderate to severe pulmonary hypertension which is attributable to an increased pulmonary precapillary resistance to flow under the influence of chronic hypoxia. The progressive development of medial hypertrophy in small pulmonary arteries and arterioles under the influence of chronic hypoxia is believed to further contribute to the increased vascular resistance.

Zusammenfassung – Das spontane Auftreten von Stauungsinsuffizienz des rechten Herzens (Hochgebirgs- oder Brisket-Krankheit) bei Rindern in grosser Höhe gibt einen Hinweis auf die Belastung bei der Höhenanpassung dieser Tiere. Rinder aus niedrigen Höhen leiden in Höhen von 3000 m und höher an leichter bis schwerer pulmonaler Hypertonie. Sie ist Folge eines Anstiegs des präkapillaren Gefässwiderstandes in den Lungen bei chronischer Hypoxie. Die progressive Entwicklung einer Mediahypertrophie in den kleinen Pulmonalarterien und Arteriolen bei chronischer Hypoxie trägt wahrscheinlich zusätzlich zu dem Anstieg des Gefässwiderstandes bei.

Résumé – L'appartion spontanée d'une insuffisance de compression dans le ventricule droit du coeur (mal de montagne ou de Brisket) chez le bétail soumis aux hautes altitudes montre la tension subie par ces bêtes lors de leur acclimatation à l'altitude. Le bétail de plaine souffre, aux altitudes supérieures à 3000 m, d'une hypertonie pulmonaire légère ou grave. Elle est la conséquence d'un accroissement de la résistance des vaisseaux précapillaires des poumons par hypoxémie chronique. Le développement progressif d'une hypertrophie des petites artères pulmonaires et des artérioles dans le cas d'une hypoxémie chronique accroît probablement encore la résistance des vaisseaux.

THE fact that domestic breeds of cattle have difficulty in adapting to high altitude environment has indirectly been recognized for years by the existence of high mountain or *brisket disease* within this species. This syndrome is a non-infectious disease of cattle residing at high mountainous altitudes and is characterized by severe pulmonary hypertension and concomitant congestive right heart failure.

The disease has been recognized in the high mountain valleys of Colorado since the end of the 19th century. There is some evidence that it was seen in the cattle of Spanish conquestadores during the South American expeditions of the 16th century. The first report in modern literature pertaining to this malady was by Glover and Newsom in 1915.

High mountain disease is recognized in the Rocky Mountains of North America (Colorado, Utah, Wyoming) and the Andes Mountains of South America (Columbia, Peru). The syndrome develops in animals resident at altitudes above approximately 7000 ft. The overall incidence of the disease is estimated to be 0.5 to 2 per cent of the cattle above this altitude with direct relationship existing between resident altitude and incidence. All ages and both sexes are affected, although in Colorado a higher incidence is seen in animals under 1 year of age. The occurrence of the clinical syndrome appears to be higher in animals newly imported into the high altitudes than in the native cattle. In Colorado there is a definite seasonal variation in the incidence of the disease with the occurrence being highest in the fall, winter, and early spring. Clinical cases are frequently noted to develop following a period of inclement weather.

FIG. 1. Calf with clinical high mountain disease showing subcutaneous edema

The management practices of the mountain ranches of the Western United States consist of spring calving, mountain grazing during the summer months, and valley meadow grazing in the fall, winter, and spring, with supplemental feeding of hay and seed oil meals during the winter. In areas where high mountain disease occurs, the altitude of the winter range may vary from 6000 to 10,000 ft and the summer range from 7000 to 10,500 ft. In these areas of the United States the climate is temperate with cool, dry summers, cold winters, and marked daily variations in temperature.

Clinical signs in an affected animal include subcutaneous edema especially in in the ventral pectoral, and cervical areas, distention and pulsation of the jugular vein, ascites, and frequently a profuse, fluid diarrhea (Fig. 1). The animals tend to show labored breathing and upon forced exertion may collapse and die. Affected animals have been shown to have severe pulmonary hypertension (Hecht *et al.*, 1959; Will *et al.*, 1962) and failure of the right side of the heart. Removal of affected animals to lower elevations results in spontaneous clinical recovery in approximately 50 per cent of the cases.

Pathologically, affected animals show generalized passive congestion and edema, hydrothorax, ascites and cor pulmonale. Postmortem pulmonary arteriography shows decarbonization of the pulmonary arterial tree indicative of an increased precapillary resistance to flow (Alexander and Jensen, 1963a). Histopathological

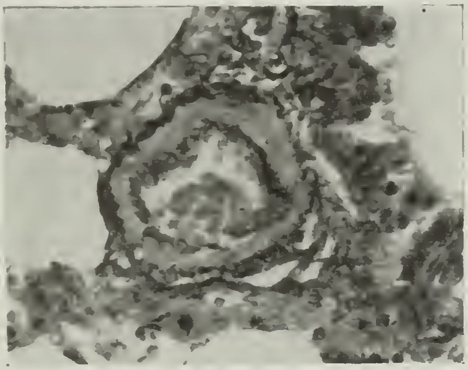

FIG. 2a. Normal small pulmonary artery 60 μ in diameter. Verhoeff-van Gieson stain, 620

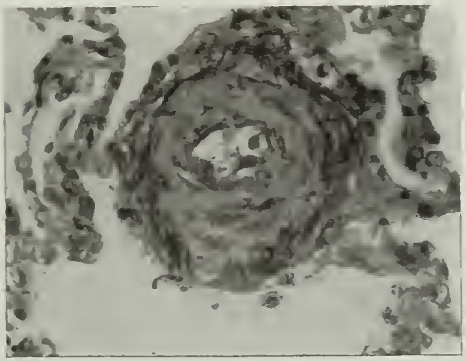

FIG. 2b. Small pulmonary artery, 60 μ in diameter, showing medial muscular hypertrophy from an animal with high mountain disease. Compare with Fig. 2a Verhoeff-van Gieson stain, 620

examination of the lungs (Alexander and Jensen, 1963b, c) reveals that the most constant alteration is medial smooth muscle hypertrophy and adventitial proliferation around the small pulmonary arteries and arterioles (Fig. 2). Distal occlusion of small arteries by thrombi, emboli, or intimal proliferations is not present, and there is no morphological evidence of postcapillary obstruction.

Experimental evidence has demonstrated that normal cattle taken from a low altitude to a high altitude develop pulmonary hypertension. In one experiment (Alexander *et al.*, 1960; Will *et al.*, 1962) each of 10 animals, originating from an elevation of 3600 ft, when taken to an altitude of 10,000 ft for 6 months, developed significant pulmonary hypertension of varying magnitudes (Fig. 3). In two of the animals right heart failure ensued. In the absence of significant increases in flow, blood viscosity, and pulmonary arterial wedge pressure, the increased vascular

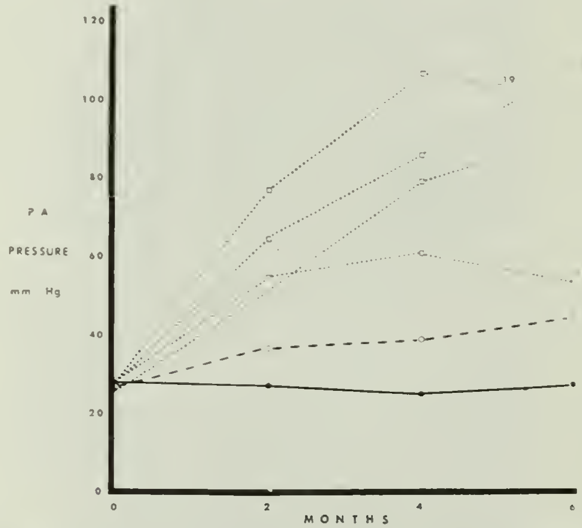

FIG. 3. Mean pulmonary arterial pressure response in experimental cattle at high and low altitudes. Ten control animals at 5000 ft ——● and ten animals at 10,000 ft. – – – – –○ moderate hypertension (6) ....☐ severe hypertension (4)

resistance was attributed to a decrease in the cross sectional area of the pulmonary vascular bed at the precapillary level. Chronic hypoxia was incriminated as the primary etiologic factor. Histopathological study of lungs from these cattle quantitatively demonstrated medial muscular hypertrophy in the small arteries and arterioles proportional to the degree of hypertension (Alexander and Jensen 1963d). In a subsequent study (Grover *et al.*, 1963) 9 weeks at an altitude of 12,700 ft produced significant pulmonary hypertension in 10 cattle originating from an altitude of 3500 ft, with one animal developing congestive right heart failure. Thus a further increase in resident altitude from 10,000 to 12,700 ft hastened the development of pulmonary hypertension, although the atmospheric PO_2 is only 10 mm Hg less at the higher altitude, thus indicating the apparent extreme sensitivity of the bovine pulmonary vasculature to changes in oxygen tension.

The magnitude of the pulmonary hypertension which develops when cattle from low altitude are moved to high altitude varies. The normal mean pulmonary arterial pressure in cattle at 5000 ft is 25 to 30 mm Hg. When moved to high altitudes some animals develop only moderate pulmonary hypertension (mean pressures of 40–55 mm Hg), while in others the pressure continues to rise with time until mean values of 75–110 mm Hg are reached. A recent study in progress (Will and Alexander) indicates that normal cattle native to and resident in the high altitudes (10,000 ft) have mean pulmonary arterial pressure in the moderate hypertensive range of 35–50 mm Hg. This magnitude of pulmonary arterial pressure has been found to be present in all animals studied thus far, irrespective of age.

When gaseous mixtures simulating altitudes of 10,000 to 20,000 ft are administered to cattle for short durations, a rise of only approximately 10 mm Hg is noted in the pulmonary arterial pressure (Kuida *et al.*, 1962; Grover *et al.*, 1963). This response to acute hypoxia is similar to that seen in man and other species. Cattle do not, therefore, demonstrate their apparent greater reactivity to hypoxia upon acute exposure. This moderate hypertensive response to acute hypoxia is similar to the rise in pressure observed in cattle during their first few days resident at high altitude (Grover *et al.*, 1963). Conversely, when 100 per cent oxygen is administered to animals which have severe or moderate high altitude induced pulmonary hypertension, the pulmonary arterial pressure is markedly lowered, but not to control levels.

These observations indicate that the early rise in pressure seen when animals are moved to a hypoxic environment is related to the vasoconstrictive effect of the lowered atmospheric PO_2, but that the subsequent progressive rise in pressure and resistance appears related to the development of organic vascular changes such as medial hypertrophy within the small pulmonary arteries and arterioles. Support for this interpretation is gained from the observation that when cattle with high mountain disease are moved to low altitude there is an immediate decrease in pulmonary arterial pressure, but not to normal levels. This is followed by a slow decline in pressure over a period of months until normal values are obtained. The initial decline in pressure appears related to the higher atmospheric oxygen tension at the lower altitude relieving the vasoconstrictive influence, while the latter could be interpreted as a gradual reversal of the organic vascular changes. Studies are now in progress relative to this hypothesis.

It therefore appears that the pathogenesis of the high altitude induced pulmonary hypertension, and thus bovine high mountain disease, appears directly related to chronic hypoxia. The manner and mechanism whereby low atmospheric oxygen tension influences the pulmonary vessels is not known. Initially this stimulus appears to cause vasoconstriction of the pulmonary arterioles. This in turn is followed by medial muscular hypertrophy and adventitial proliferation in these precapillary vessels. These changes in themselves, possibly combined with augmented vasoconstriction, appear to be able to further increase the pulmonary vascular resistance, and in certain instances result in cardiac failure.

The reasons why one animal will develop severe pulmonary hypertension at high altitude and another animal only moderate hypertension is at present unknown. It has been noted that even though cattle taken to high altitude show some arterial oxygen desaturation, the level is similar in all animals and not related to the degree of hypertension (Will *et al.*, 1962). Similarly data on blood oxygen tensions in cattle at high altitude do not serve to explain the variable hypertensive responses (Grover *et al.*, 1963). There have been indications that genetic make-up of individual breeds and animals may play some role in their susceptibility to the disease. In addition cardiac failure might ensue if primary pulmonary parenchymal disease is superimposed upon an animal with moderate pulmonary hypertension.

The adaptative advantage at high altitude that would result from the development of moderate pulmonary hypertension in cattle is uncertain and remains for conjecture, although there is some evidence (Fowler and Read, 1963) that in man it might result in a beneficial redistribution in pulmonary blood flow. The disadvantages of severe pulmonary hypertension with the development of congestive right heart failure are obvious and indicates a failure to adjust to the environment. Thus it is apparent that the commonly domesticated breeds of cattle do not appear to be particularly adaptable to high altitude environment. Certain inherent features or undesirable potentials may therefore play a role in this evident lack of altitude adaptability.

It has been demonstrated that normal cattle possess rather large amounts of smooth muscle in the small pulmonary arteries and arterioles (Alexander and Jensen, 1963a). Although this smooth muscle does not display an exaggerated contractile response at acute hypoxia, it apparently readily undergoes hypertrophic changes when the hypoxic stimulus is maintained in a high altitude environment. It is believed that this hypertrophy significantly contributes to the development of both the moderate and severe pulmonary hypertension observed at high altitude.

Contrary to man and certain other species, cattle do not show a sustained hyperventilatory response at high altitude. An initial increase in ventilation has been demonstrated in cattle at high altitude, but this response lasted for only about one week and then returned to low altitude values (Grover *et al.*, 1963). It appears therefore that cattle, for reasons currently unknown, do not employ this important adaptative mechanism and thus allow for greater hypoxemia.

Finally, cattle do not develop a significant erthropoeitic response under the stimulus of decreased atmospheric PO_2 (Will *et al.*, 1962; Will and Alexander). Both hemoglobin and hematocrit values show only slight increases with no appreciable alteration noted in total plasma volume. This minimal response differs from that in man and other species subjected to the same environment.

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DIE LOKALE GEHIRNDURCHBLUTUNG BEI CHRONISCHEM SAUERSTOFFMANGEL

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Abstract – The effect of acute and chronic intermittent hypoxia on cerebral blood flow was investigated in cats. Heat conductivity sounds were implanted in the thalamus or hypothalamus where they remained for several months. Two groups of 10 cats were exposed for 4 hr daily to 10% and 8% O_2 respectively. Cerebral blood flow increased greatly at 8% O_2 and fell little during the exposure time. The response was less marked on the following days, but even after 20 days an increase of cerebral blood flow was seen. At 10% O_2 no circulatory response was seen after 10 days exposure. During the course of adaptation the response of blood flow did not decrease linearly, but followed the pattern of a reactive periodic. There was a moderate increase of RBC, hematocrit and hemoglobin in the blood.

Zusammenfassung – Bei Katzen wurde die Wirkung von akutem und chronisch-intermittierendem O_2-Mangel auf die lokale Gehirndurchblutung untersucht. Zur Registrierung der Gehirndurchblutung wurden Wärmeleitsonden in den Thalamus oder den Hypothalamus implantiert. Die Sonden blieben mehrere Monate lang im Gehirn. Je 10 Katzen wurden 10% bzw. 8% O_2 in der Atemluft mindestens 4 Stunden täglich ausgesetzt. Bei 8% O_2 stieg die Gehirndurchblutung stark an und sank im Verlauf des O_2-Mangels geringfügig ab. In den folgenden Tagen war die Durchblutungssteigerung geringer, doch war sie auch nach 20 Tagen noch nachweisbar. Bei 10% O_2 trat nach 10 Versuchstagen keine durch O_2-Mangel bedingte Durchblutungsreaktion mehr auf. Die Gehirndurchblutung fiel im Verlauf der Anpassung nicht gleichmässig ab, sondern in Form einer reaktiven Periodik. Im Blut war ein geringer Anstieg von Erythrozytenzahl, Hämatokrit und Hämoglobin zu beobachten.

Résumé – On a examiné l'influence d'un manque prononcé ou chronique, mais intermittent d'oxygène sur la vascularisation sanguine locale du cerveau de chats. Afin d'enregistrer cette vascularisation, on a implanté des sondes thermiques dans le thalamus ou l'hypothalamus. Ces sondes sont restées plusieurs mois dans le cerveau. On a exposé des groupes de 10 chats au moins 4 heures par jour à des atmosphères ne présentant que 10 ou 8% d'oxygène. Lors de l'exposition à une atmosphère ne comportant que 8% d'oxygène, la vascularisation augmenta brusquement pour ne rediminuer que lentement avec le temps. Cet effet fut moins prononcé les jours suivants, mais était encore sensible après 20 jours. A une concentration en O_2 de 10%, on ne remarquait plus de réaction caractérisée après 10 jours d'essais. La vascularisation du cerveau n'a pas diminué régulièrement au cours des essais, mais a présenté des paliers périodiques. On a constaté une faible augmentation du nombre des érythrocytes, de l'hématocrite et de l'hémoglobine.

NACH Untersuchungen von Lennox u. Gibbs (1932), Opitz (1941), Noell u. Schneider (1942, 1943), Schneider (1953), Sokoloff u. Kety (1960) u. a. führt akuter Sauerstoffmangel zu Steigerungen der Gehirndurchblutung. Bei allmählicher Verminderung des Sauerstoffs in der Atemluft kommt es nach Noell u. Schneider (1943) bei 11% O_2 in der Atemluft zu den ersten Durchblutungsänderungen. Dabei steigen auch Blutdruck, Herz- und Atemfrequenz an. Bei weiterer Verminderung wird die Gehirndurchblutung bis zu einem Maximum erhöht; danach kommt es unter den Erscheinungen eines Kollaps zu steilem Abfall der cerebralen Durchblutung. Es gibt erhebliche interindividuelle Unterschiede im Ertragen von akutem Sauerstoffmangel, und es ist möglich, sich an einem Sauerstoffmangel anzupassen. Anpassungsvorgänge von Kreislaufgrößen, z. B. des Herzminutenvolumens (Barcrofft, 1927; Grollman, 1930) oder der Muskelgefäße (Clark *et al.*, 1955; Valdivia, 1956) wurden objektiviert, und bei morphologischen Untersuchungen der Gehirnkapillaren bei langdauerndem Sauerstoffmangel fanden sich ebenfalls Hinweise auf Anpassungsvorgänge. (Mercker u. Schneider, 1949; Mercker u. Opitz, 1949).

Über die Dynamik der Änderungen in der Gehirndurchblutung bei chronischem O_2-Mangel is bisher nichts bekannt, was vorwiegend auf methodische Schwierigkeiten zurückzuführen ist.

Mit Hilfe von chronisch implantierten Wärmeleitsonden (Betz u. Hensel, 1962), konnte die Durchblutung im Bereich des Thalamus und des Hypothalamus bei wachen, frei beweglichen Katzen über mehrere Monate fortlaufend registriert werden. Mit dieser Methode gelang es, die Gehirndurchblutung beim akuten und beim Übergang in den chronischen Sauerstoffmangel zu erfassen.

METHODE

Die Methode beruht auf der Messung des Wärmetransports von einem im Gehirn implantierten Thermoelement, dessen eine Lötstelle mit Wechselstrom konstant aufgeheizt wird. Bei bekannter Eichkonstanten K wird die Temperaturdifferenz (ϑ) zwischen der mit Wechselstrom (I^2) konstant aufgeheizten Lötstelle und einer zweiten nicht geheizten Lötstelle, die in definiertem Abstand zur ersten ebenfalls im Gehirn angeordnet ist, fortlaufend registriert. Die Wärmetransportzahl

$$\lambda' = \frac{K \cdot I^2}{\vartheta}$$

ist dann ein Maß der lokalen Durchblutung. Für die Durchblutungsmessungen im Gehirn wurden die Lötstellen des Thermoelements in 2 getrennten Nadeln untergebracht, und stereotaktisch in bilateral symmetrische Stellen des Thalamus oder Hypothalamus implantiert. 4–6 Wochen nach der Operation, nachdem die Sonden gut eingeheilt waren, wurden die Versuchstiere in eine verglaste Kammer gebracht und einem Sauerstoffmangel unterschiedlicher Stärke und Dauer ausgesetzt. Die Versuchskammern waren ventiliert, den Sauerstoffgehalt der Luft kontrollierten wir mit einem Oxymeter (nach Beckmann). CO_2 wurde fortlaufend über ein Grundumsatzgerät der Fa. Hartmann und Braun mit aufgezeichnet; durch Absorption des CO_2 wurde dafür gesorgt, daß keine unerwünschten Nebenwirkungen des CO_2 auftraten.

ERGEBNISSE

Änderungen der Gehirndurchblutung bei akutem Sauerstoffmangel

Bei 10 Versuchstieren wurde durch Einleiten von Stickstoff in den Versuchskasten der Sauerstoffgehalt der Atemluft allmählich vermindert. Die Geschwindigkeit der Verminderung des Luftsauerstoffs war bei allen Tieren gleich und betrug

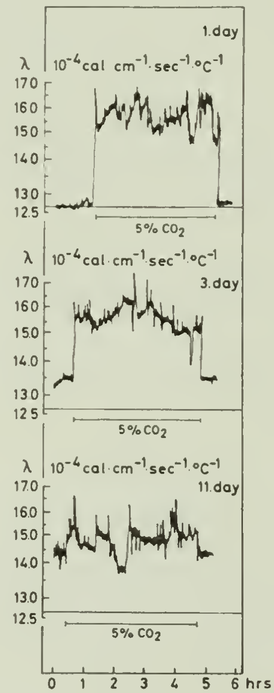

Abb. 1. Durchblutungserhöhung im Thalamus und Hypothalamus bei 10 Katzen unter Verminderung des Luft-Sauerstoffs. Die Verminderung betrug 0,5% O_2/min

1–2%/min. Die auftretenden Durchblutungsänderungen im Hypothalamus und Thalamus mit ihren Streuungen sind in der Abb. 1 aufgezeichnet. Die ersten Durchblutungsänderungen begannen bei 15% O_2 in der Atemluft. Es kam zum Durchblutungsanstieg mit Erreichen des Maximums zwischen 7 und 6% O_2. Wurde der Sauerstoffmangel weiter verstärkt, kam es zu einem Wiederabfall der Durchblutung und gleichzeitigem Blutdruckabfall. Diese Reaktionen sind durch CO_2 deutlich zu beeinflussen.

Unter gleichzeitiger Gabe von CO_2 stieg die Durchblutung stärker an als bei Absorption des gesamten Kohlendioxyds.

Chronischer Sauerstoffmangel

Die Reaktionen auf chronisch durchgeführten Sauerstoffmangel unterscheiden sich initial nicht von denen beim akuten Sauerstoffmangel. Es kam ebenfalls zu einem Anstieg der Gehirndurchblutung wie in der Abb. 1, Herzfrequenzsteigerung und eine Tachypnoe.

(a) Versuche bei 10% Sauerstoff in der Atemluft.

Die Abb. 2 zeigt einen Versuch, in welchem ein Tier täglich 4 Stunden lang einem Sauerstoffmangel ausgesetzt war. Es ist zu erkennen, daß schon am ersten Tag einige Stunden nach Beginn des Versuchs ein Wiederabsinken der

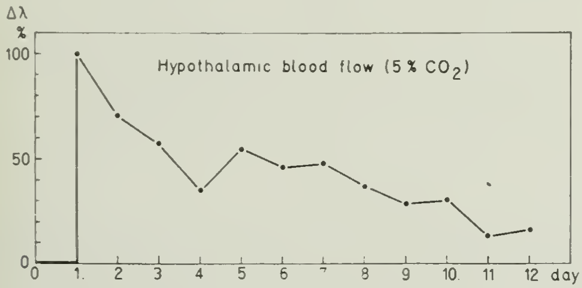

Abb. 2. Hypothalamusdurchblutung einer Katze am 1., 3. und 5. Tag eines Sauerstoffmangelversuches. 10% O_2 in der Atemluft täglich 4 Stunden lang. Neben den Durchblutungsänderungen durch O_2-Mangel am 1. und 3. Tag sind in den Kurven spontane und reaktive kurzfristige Durchblutungsschwankungen erkennbar

zunächst stark gesteigerten Gehirndurchblutung auftrat. Am dritten Tag war auch der Anstieg schon geringer geworden, und am fünften Tag stieg die Durchblutung nicht mehr über den Ausgangswert des ersten Tages hinaus. Es ist außerdem zu erkennen, daß der Ausgangswert der Durchblutung im Verlauf der täglich durchgeführten Versuche gering absank. Bei einer Serie von 5 Tierversuchen über jeweils 12 Tage, in welchen die Tiere täglich 4 Stunden einem Sauerstoffmangel von 10% in der Atemluft ausgesetzt waren, war deutlich erkennbar, daß die Durchblutung des Hypothalamus, welche in der Abb. 3 als Mittelwert über die gesamte Versuchszeit dargestellt ist, nach 12tägiger Exposition nicht mehr anstieg.

(b) Wurden die Tiere einem Sauerstoffmangel von 8% O_2 in der Atemluft ausgesetzt, so war die initiale Steigerung höher als bei 10% O_2. Ähnlich wie unter 10% O_2 kam es auch bei dieser Gruppe zu einem allmählichen Absinken der initial hohen Gehirndurchblutung, jedoch verlief die Änderung langsamer und erreichte bei den meisten Tieren innerhalb von 12 Tagen nicht wieder den Ausgangswert (Abb. 4), sondern blieb im Mittel etwas erhöht.

Wurde der Sauerstoffmangel jedoch ohne Unterbrechungen durchgeführt, so sank meist auch bei 8% O_2 in der Atemluft die Gehirndurchblutung wieder auf den Ausgangswert ab.

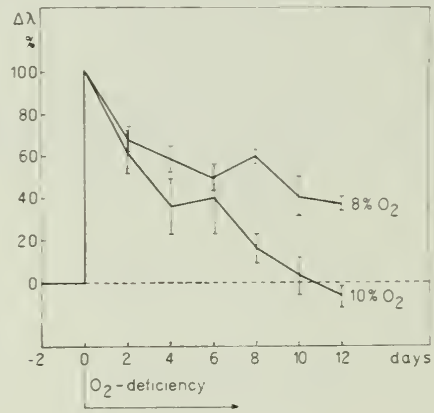

Abb. 3. Mittlere Gehirndurchblutung (mit SE) bei 12 tägigem O_2-Mangel täglich 4 Stunden lang mit 10% O_2. (5 Katzen). Die Änderung der Wärmetransportzahl des 1. Versuchstages (= Durchblutungssteigerung) ist als 100% Änderung vom Durchblutungsausgangswert in atmosphärischer Luft angegeben (% $\Delta\lambda$)

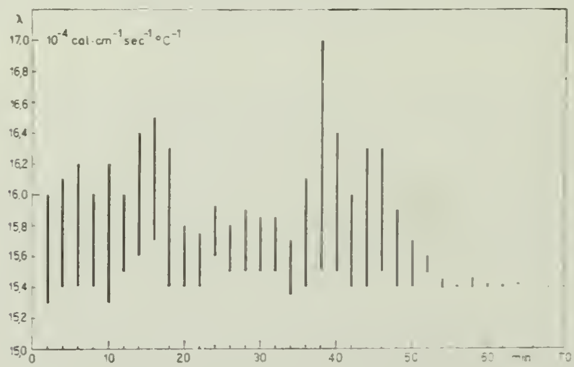

Abb. 4. Gehirndurchblutungsänderungen mit Streuung bei 5 Versuchstieren bei 12tägigem Sauerstoffmangel, 4 Stunden täglich. Die Meßpunkte und Koordinaten sind ebenso gewonnen wie in Abb. 3.

Sowohl bei den Kurven, die die Änderung der Gehirndurchblutung bei 10% O_2 als auch bei denen, die die Änderungen der Gehirndurchblutung bei 8% O_2 darstellen, ist deutlich zu erkennen, daß der Abfall der Gehirndurchblutung nicht gleichmäßig vor sich ging, sondern daß die Kurvenzüge Unterbrechungen ihrer nach unten gerichteten Tendenz aufwiesen. Die nach oben gerichteten Rückschwingungen der Kurven traten zwischen dem 3. und 6. Tag und dann noch einmal am 8. oder 10. Tag auf. Sie waren interindividuell unterschiedlich deutlich und konnten in einzelnen Fällen den Wert des 1. Tages wieder erreichen (Einzelversuch, Abb. 5).

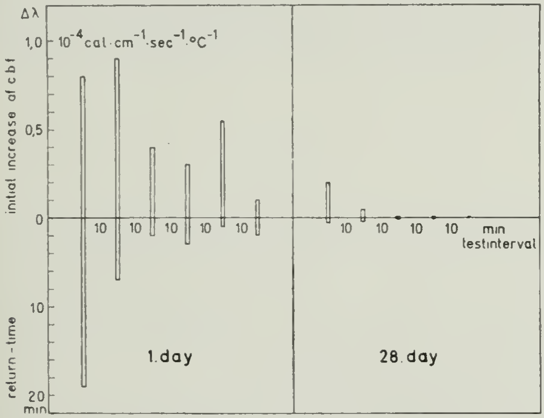

Abb. 5. 8 und 10% O_2 in der Atemluft einem Tier alternierend zugeführt. Sowohl an den Versuchstagen mit 8% O_2, als auch den Tagen mit 10% O_2, zeigte sich, daß die Durchblutungsverminderung im Verlauf der gesamten Versuchszeit nicht gleichförmig war

DISKUSSION

Die Änderungen der Gehirndurchblutung während des chronischen Sauerstoffmangels fassen wir als Anpassungsvorgang auf. Da bei der Anpassung an Sauerstoffmangel neben den Umstellungen im Kreislauf auch Änderungen der Atmung, Umstellungen im Mineralhaushalt, in der Wasserausscheidung, im Myoglobingehalt und anderen Funktionen auftreten, ist es schwierig zu entscheiden, ob die Erweiterung der Gehirnkapillaren, die von Mercker und Opitz (1949) bei Höhenversuchen beschrieben wurden, allein für die Anpassung der Gehirndurchblutung verantwortlich ist. Die Befunde von Hurtado (1932, 1945), Luft (1941) und Pichotka (1957) zeigen, daß es auch Anpassungsvorgänge der Gewebe gibt. Wie groß der Anteil der Umstellung des Kreislaufs der Gewebe oder der Atmung bei der Änderung der Gehirndurchblutung im Verlauf dieser Versuche ist, läßt sich kaum abgrenzen. Die Durchblutung verändert sich über mehrere Tage kontinuierlich, so daß angenommen werden muß, daß die Faktoren, welche die Gehirndurchblutungsänderung steuern, ebenfalls einem dynamischen Vorgang unterworfen sind. Das zeigte Barcrofft (1927) für das Herzminutenvolumen und Severinghaus

(1962) für die Veränderungen von P_{CO_2}. Die Änderungen dieser Größen entsprachen in ihrem zeitlichen Verlauf denen der Gehirndurchblutung. Die Änderung einer Einzelgröße wie der Gehirndurchblutung kann daher bei Fragen der Adaptation nur im Zusammenhang mit der Änderung anderer Systeme gesehen werden.

Da zahlreiche Erkrankungen des Kreislaufs, der Atmung und des Blutes mit chronischem O_2-Mangel einhergehen und da aus den Ergebnissen hervorgeht, daß Anpassungen der Gehirndurchblutung stattfinden, muß bedacht werden, daß trotz anscheinend normaler Gehirndurchblutung andersartige Reaktionen erwartet werden können als unter Verhältnissen mit normaler O_2-Versorgung.

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BLOOD OXYGEN TRANSPORT IN NEWBORN ANIMALS AT HIGH ALTITUDE

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Abstract – Observations were made on the blood oxygen transport of calves indigenous to the Central Peruvian Andes at 4200 m and at sea level, from birth to 30 days of age. There were no appreciable differences in all the functions studied at sea level and at high altitude at birth. The normal changes with age were present in both environments, but varied in degree so that by the 30th day, the high-altitude animals showed higher hemoglobin concentration and oxygen capacity than their sea-level controls.

Zusammenfassung – Der Blut-Sauerstofftransport bei zwei Gruppen von Kälbern, einheimisch in den peruanischen Anden in 4200 m oder in Seehöhe, wurde von der Geburt an bis zum Alter von 30 Tagen untersucht. Bei der Geburt bestanden keine Unterschiede in den gemessenen Funktionen zwischen den beiden Gruppen. Die normalen, altersmässig einsetzenden Veränderungen waren zwar in beiden Gruppen vorhanden, doch waren sie im Ausmass verschieden, so dass am 30. Tag die Hochgebirgstiere mehr Hgb und eine höhere O_2-Kapazität zeigten als die Vergleichstiere im Tal.

Résumé – On a examiné le transport de l'oxygène par le sang sur deux groupes de veaux: Les uns provenaient des Andes péruviennes à 4200 m d'altitude, les autres du niveau de la mer. Ces veaux furent suivis depuis leur naissance jusqu'à l'âge de 30 jours. A la naissance, on n'a constaté aucune différence fonctionnelle entre les deux groupes. Les modifications dues au développement normal se produisirent chez chaque individu, mais leur importance était différente d'un groupe à l'autre. Ainsi, au 30ème jour, les veaux d'altitude présentaient une plus haute concentration en hémoglobine et, partant, une plus forte capacité en oxygène que leurs congénères de la plaine.

THE fetus lives in an hypoxic environment, and the respiratory functions of its blood resemble strikingly those of high-altitude adapted adults (Barcroft, 1925). At sea level, birth represents a change from the hypoxic fetal life to one in which O_2 is supplied normally; but at altitude, the transition does not mean a complete reversal of the hypoxic condition. In view of this difference, it was thought interesting to compare the flow of oxygen in the respiratory circuit of newborn animals, born and reared at sea level and at high altitude, during their first month of life.

METHODS

Eleven calves of both sexes were used at sea level (Lima, Peru) and at high altitude (Pinascochas, Peru, 4,200 m), respectively. All the animals were born naturally at full-term, and were tested on the lst, 4th, 10th and 30th day of age.

Ventilatory measurements were made during three consecutive 3-min periods by the open circuit technique, using a specially fitted mask. For the estimation of the oxygen consumption, the expired air was collected by the Douglas bag technique and analyzed by the method of Scholander (1947). Blood was obtained anaerobicly from a branch of the subclavian artery and from the jugular vein. The O_2 content of the blood as drawn and after equilibration (at 38° C) at $PCO_2 = 40$ mm Hg and $PO_2 = 200$ mm Hg (oxygen-carrying capacity) and $PO_2 = 25$ mm Hg (one point on the oxyhemoglobin dissociation curve) was determined by the manometric method of Van Slyke and Neill (1924). Total hemoglobin and percent O_2 saturation were calculated from the O_2 capacity. O_2 physically dissolved was taken as: $0.026(PO_2)/760 \times 100$.

RESULTS

Ventilation

At birth there were no significant differences in the respiratory rates of these calves at sea level and at high altitude, but minute and tidal (calculated) volumes were significantly smaller at high altitude than at sea level. Four days later, rate and minute ventilation were reduced slightly at sea level, but elevated significantly at altitude. The respiratory rate on this day was higher in the altitude-born calves than in the sea-level animals, but the ventilatory minute volumes were not dif-

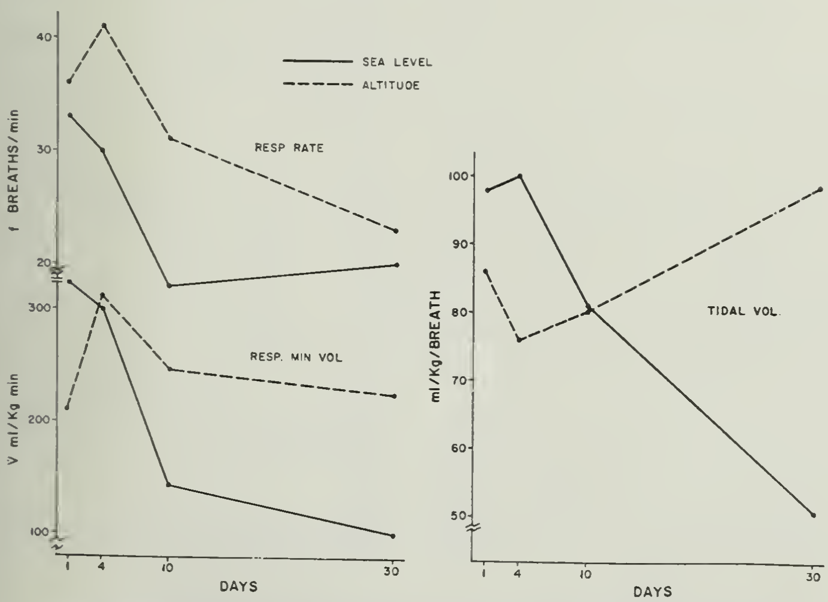

FIG. 1. The respiratory rate, minute ventilation and tidal volume of calves during the first month of life at sea level and high altitude

ferent. Tidal volume, on the other hand, decreased at altitude in this interval and was significantly lower than at sea level, where it did not change. At both altitudes, respiratory rate and minute volume declined thereafter significantly until the tenth day, but the fall was not so large in the altitude animals, so that both these functions were significantly higher on this day in these animals than in the controls. From the tenth to the thirtieth day, the respiratory rate at sea level changed no further while the minute volume continued to decline, whereas at altitude, the minute volume was stabilized while the rate continued to fall; so that on the thirtieth day, the respiratory minute volume was significantly higher at altitude than at sea level, while the respiratory rates were not different. Tidal volume at sea level decreased, and at high altitude increased, steadily from the fourth day onward, resulting in equal values on the tenth day, but significantly higher at altitude than at sea level on the thirtieth day. These results are illustrated in Fig. 1.

O_2 Uptake

The rates of oxygen consumption of these calves were related directly to the corresponding minute ventilations, at sea level and at high altitude, respectively. Thus, the oxygen consumption was significantly lower at birth, but higher at all

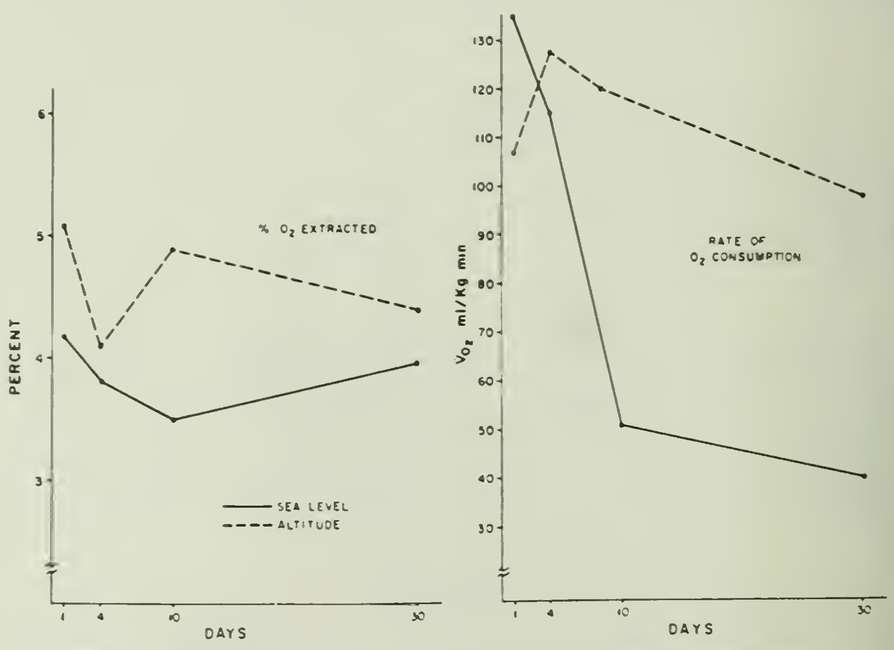

FIG. 2. The O_2 uptake and the rate of oxygen consumption of calves during the first month of life at sea level and high altitude

the other ages in the high altitude than in the control calves (Fig. 2). The percent of O_2 extracted from the inspired air was higher at altitude. The ventilation equivalent of oxygen was lower at altitude than at sea level on all the days.

The Blood

At birth there were no significant differences in the oxygen content of the arterial blood as drawn, the oxygen-carrying capacity and the total hemoglobin; All these functions fell significantly in the first four days of life, then increased again in the next six days, and thereafter stabilized; in both environments, but at high altitude, the fall, first, was less large and the recovery, later, more extensive, so that these factors were significantly higher in the altitude-reared calves than in the sea-level controls, from the fourth day onward (Fig. 3). Arterial oxygen saturation was reduced at altitude from the tenth day onward.

Venous O_2 content and saturation were significantly lower at altitude than at sea level on all the days, except the first, when they were not different. These functions fell sharply at altitude in the first four days, then remained stable until the tenth day, in contrast to sea level where there occurred a gradual and not so large decline through the tenth day. Thereafter, $C_{V_{O_2}}$ and saturation increased

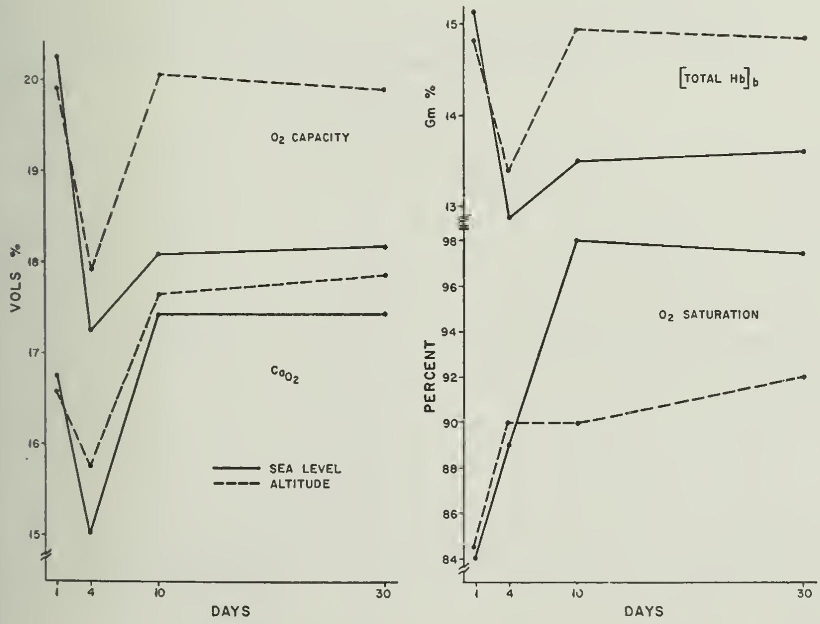

FIG. 3. The O_2 content, saturation, capacity and total hemoglobin of arterial blood of calves during the first month of life at sea level and high altitude

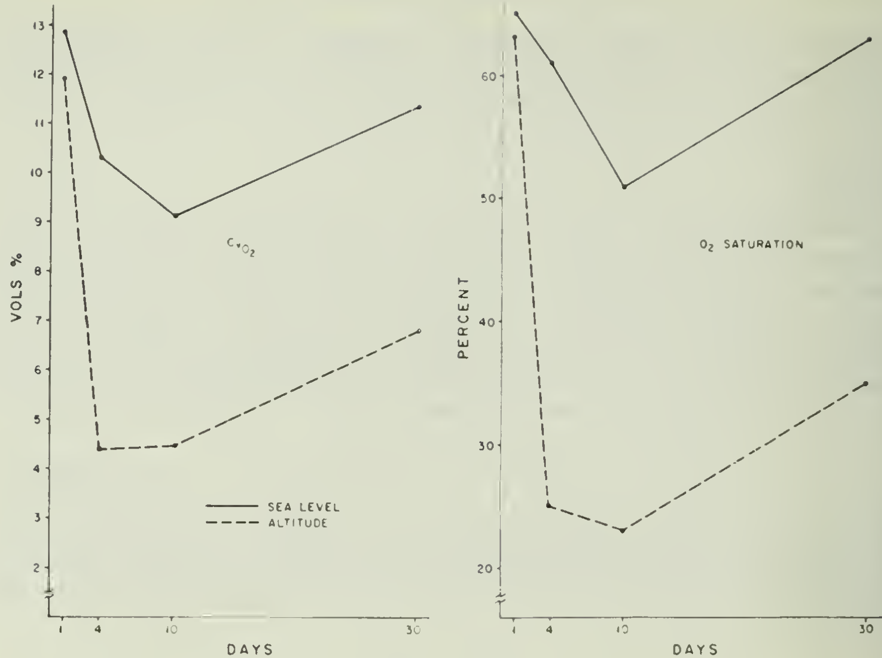

Fig. 4. Venous O_2 content and saturation of calves during the first month of life at sea level and high altitude

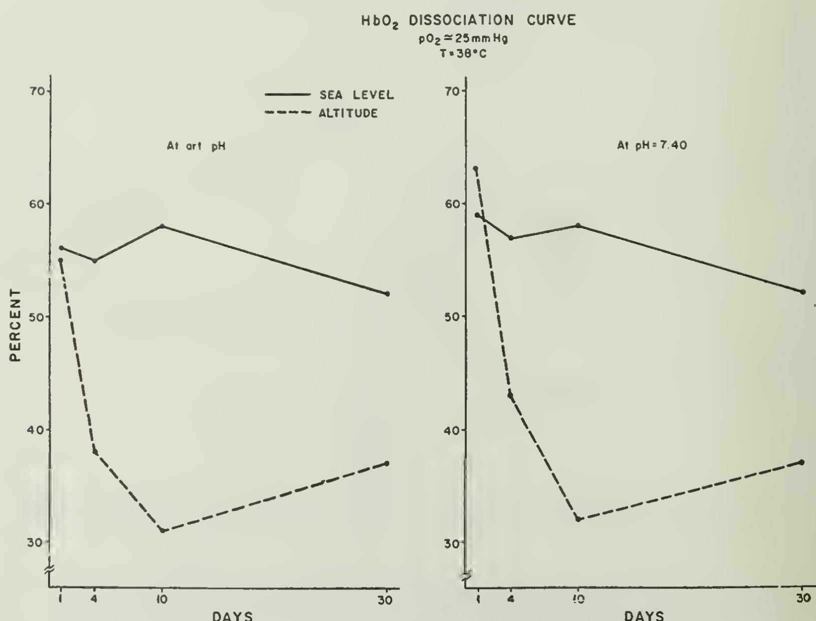

Fig. 5. The percent saturation of HbO_2 at PO_2 = 25 mm Hg (PCO_2 = = 40 mm Hg and 38° C) of the blood of calves during the first month of life at sea level and high altitude

gradually and at the same rate in both environments until the thirtieth day (Fig. 4). Hence, the A–V O_2 difference was significantly greater in these calves at high altitude than at sea level from the fourth day onward.

The percent oxygen saturation of hemoglobin at $pO_2 = 25$ mm Hg was significantly reduced, excepting on the first day, in these altitude-native calves, in contrast to the sea-level animals in which not so large shifts occurred (Fig. 5). This change at altitude in the affinity of hemoglobin for oxygen was apparently completed during the first four days of life.

Body Weight

In the present experiments, the calves weighed at birth a mean 10 Kg less at altitude than at sea level. A consistent and steady weight gain from birth of approximately 400 g/day was shown by the sea-level animals. The altitude-born calves displayed no significant weight gain in the first four days, but thereafter grew steadily and at a faster rate (approximately 600 g/day) than the sea-level controls.

DISCUSSION

The present experiments indicated that there were no significant differences at birth in all but two of the factors measured in this study, namely: (1) the minute volume of ventilation and (2) the rate of oxygen consumption, which were reduced at altitude.

The absence of an O_2 drive during the first day of life has been reported previously (Miller and Smith, 1955; Girard, Lacaisse and Dejours, 1960; Adolph and Hoy, 1960). On the other hand, Dawes and Mott (1959) and Cross (1961) observed in newborn rabbits and infants, respectively, an increase of ventilation when their subjects breathed an hypoxic mixture, and Adamsons (1959) found that 10% O_2 induced in newborn rabbits a well maintained hyperpnea in a thermo-neutral environment, but, not so in a cool environment. Similarly, it is now known that the minimal O_2 consumption (at a neutral temperature) is not altered by moderate hypoxia, whereas the O_2 consumption response to a cool environment is invariably decreased (Hill, 1959; Dawes, 1961; Blatteis, 1963a). Under the conditions of the present experiments, the mean temperature at Pinascochas was 9° C. Hence, the depressed ventilatory and metabolic responses of the altitude-born calves on the first day of life may have been conditioned by their thermal environment. By the same token, presumably, the respiratory rate in these animals also was depressed at birth, for, if the sea-level pattern of respiration may be taken as the normal process during the first days, extrapolation of the rate would yield a significantly higher value than that observed here.

On the fourth day of life, on the other hand, there was a significant increase of the minute ventilation and, concomitantly, of the rate of oxygen consumption in the altitude-reared calves, suggesting that, by then, the O_2 drive was operating.

This concurs with the findings of Cross and Warner (1951) and Girard, Lacaisse and Dejours (1960) in infants older than 1 day. It is interesting to note, in this regard, that the hyperventilation of altitude in these calves apparently was mediated on this day largely through an increased frequency of breathing, while by the thirtieth day it was mostly due to an increased depth of respiration, viz. the same progression as in newcomers to altitude (Hurtado, 1959). At sea level, minute ventilation appeared to be regulated throughout the first month of life principally by the respiratory rate.

The rate of oxygen consumption also increased after the first day, concomitantly with the minute ventilation, indicating that the hypoxic depression of the metabolic response to cold is reversible, in agreement with the findings in other species (Blatteis, 1963b).

The blood factors all were typically elevated at birth, but not different in the sea-level and high-altitude calves. They decreased in the first four days and increased in the next six, in the usual postnatal sequence (Smith, 1959), correlatively in both environments. However, in the altitude-reared calves, the fall of, as for instance, arterial O_2 content, was smaller and the increase larger due to the compensatory hyperpnea, and was reflected in a greater oxygenation of the arterial blood after the fourth day. Similarly, the hemoglobin content increased significantly more at altitude than at sea level after the fourth day, raising the oxygen capacity and counteracting the lowered saturation of the arterial blood of these animals.

Venous O_2 content at altitude, however, was not elevated concomitantly with the arterial O_2, despite the hyperpnea and the increased hemoglobin, presumably because the oxygen consumption of these animals was increased (in response to the lower ambient temperature). Thus, the increased demand for oxygen apparently was met by a greater deoxygenation of oxyhemoglobin in the tissue capillaries, producing a larger drop in the percent saturation. This latter finding was in contradiction to Grover *et al.* (1963), who showed a narrowing of the A–V O_2 difference (and a fall in O_2 uptake) in steers taken to 12,700 ft, but their animals appeared not to have been stimulated by the cold. In the present experiments, the greater unloading of O_2 to the tissues in the altitude-born calves was achieved by a reduction in HbO_2 saturation at $PO_2 = 25$ mm Hg, a compensation apparently initiated under these conditions during the first four days of life. These events probably were further complicated by the lowering of body temperature, secondary to the decreased oxygen consumption at birth.

These results suggested that the newborn calf, despite the known greater resistance to hypoxia of newborn animals generally (Himwich *et al.*, 1941) and irrespective of his hypoxic fetal environment particularly, even when the mother was a permanent resident of altitude, was not "congenitally acclimatized" to 4200 m. The altitude-born animal seemed first to undergo the physiological adjustments ensuing from neonatal existence, in the same manner as his sea level counterpart, and, secondarily, to compensate for the supervening stimuli of hypoxia and cold.

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The principles of laboratory animal care as promulgated by the National Society of Medical Research were observed.

CHANGES IN BODY WEIGHT AS A PARAMETER OF FITNESS IN MICE EXPOSED TO DIMINISHED ATMOSPHERIC PRESSURE

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Abstract – Male mice were exposed to low atmospheric pressures, either (1) for two periods of 4 days at 425 mm Hg, before the second exposure and were allowed to regain their original body weight, or (2) for single periods of 19 days at either 540 mm, 425 mm or 380 mm Hg. In the first experiment the rate of weight loss on the second exposure was less than on the first, thus indicating that weight loss reflected loss in somatic fitness, rather than an adaptive response. The results of the second experiment indicate that loss in fitness is not directy related to simulated altitude and that a "threshold" pressure exists, below which acclimatization is impossible.

Zusammenfassung – Männliche Mäuse wurden im Unterdruck gehalten: (1) 2 Perioden von je 4 Tagen bei 425 mm Hg; nach der 1. Periode wurde gewartet, bis die Tiere das normale Gewicht wieder erreicht hatten; (2) Perioden von je 19 Tagen bei 540, 425 oder 380 mm Hg. Im 1. Experiment war der Gewichtsverlust nach der 2. Periode im Unterdruck geringer als nach der 1. Periode. Dies deutet darauf hin, dass der Gewichtsverlust eher den Verlust körperlicher Leistungsfähigkeit widerspiegelt als eine Anpassungsreaktion. Die Ergebnisse des 2. Experiments zeigen, dass ein Verlust der Leistungsfähigkeit nicht in direkter Beziehung zur simulierten Höhe steht und dass ein "Schwellen"-Unterdruck gegeben ist, nach dessen Unterschreitung Akklimatisation unmöglich wird.

Résumé – Des souris mâles furent exposées à de basses pressions atmosphériques: les unes pendant deux périodes de 4 jours chacune à 425 mm Hg (on a attendu, après la première période, que les sujets aient recouvré leur poids normal), les autres pendant des périodes de 19 jours à des pressions de 540, 425 ou 380 mm Hg. Dans le premier essai, la perte de poids fut plus faible lors de la seconde période que lors de la première. Ceci laisse supposer que la perte de poids indique plus une diminution de la force corporelle qu'une réaction à l'acclimatation. Les résultats du second essai montrent que la perte de poids et, partant, de force corporelle n'est pas en relation directe avec l'altitude simulée et qu'il existe un seuil de dépression au-delà duquel une acclimatation n'est plus possible.

INTRODUCTION

It is an axiom of modern biology that an animal is most fit in its natural environment and that a change in environment will involve a loss in fitness. Such a change occurs when men who normally live near sea level move to high altitudes. The resultant loss in fitness has been frequently described (Monge, 1937, 1942).

A number of studies have been made on the effects of low atmospheric pressures on the experimental animal. Most of them have been concerned with the effects upon particular homeostatic mechanisms such as the haemopoietic system (Dubin, 1935; Highman and Altland, 1949; Piliero, 1955), the adrenal cortex (Giragossintz and Sundstroem, 1937; Dohan, 1942; Langley, 1942; Langley and Clarke, 1942; Sundstroem and Michaels, 1942; Hailman, 1944) water loss (Swann and Collings, 1943) the maintenance of body temperature (Flückiger and Verzar, 1952; Verzar, 1957) or the effects upon the reproductive tract (Gordon, *et al.* 1943; Walton and Uriski, 1946; Moore and Price, 1948; Altland, 1949 a,b,c; Highman and Altland, 1949). Few of these studies have involved the prolonged exposure of animals to lowered pressures, and little or no attention has been paid to the long term effects of such exposure on overall fitness. Studies of the growth of experimental animals at different environmental temperatures (Harrison, Morton and Weiner, 1959; Barnett, Coleman and Manly, 1960) have illuminated the general problem, and have shown that weight changes can provide meaningful measures of the success of thermal adaptation.

As an initial investigation into the effects of simulated high altitude on somatic fitness it seemed worthwhile, therefore, to study the weight responses to varying atmospheric pressures, and since such conditions can cause a marked loss of weight in adult animals it seemed reasonable to suppose that this parameter might afford information about the extent of high altitude adaptation.

In any study of the effects of varying environmental conditions on body weights, the interpretation of the results, in terms of the reaction of the animal to its environment, is crucial (Harrison, 1959). Thus, weight changes might be exclusively adaptive in nature, conveying no direct information about overall fitness, or on the other hand they might be solely indicators of changes in fitness itself. They may also, of course, represent, to varying degrees, both fitness and adaptation. It is obvious that a solution of this problem with respect to environmental air pressure is a necessary prerequisite to the study of the comparative effects of varying pressures.

It is to be expected that if acclimatization to a given atmospheric pressure has any beneficial effect on the responses to subsequent exposure to that pressure, then adaptive mechanisms would be brought into play more rapidly on the second occasion and fitness therefore lost more slowly. In other words, if the weight loss is adaptive in nature one would expect it to be more rapid on the second exposure than on the first, whereas if the weight changes reflected changes in fitness, they should occur more slowly on the second exposure.

Whatever the significance of weight changes there is no reason to suppose that their extent would necessarily be linearly related to the atmospheric pressure; indeed, there is a considerable body of evidence that in man there are qualitative differences in response above and below "threshold" altitude, which lies around 18,000 ft (5486 m) (Pugh and Ward, 1956). It was, therefore, decided to study the body weight responses of animals exposed to three levels of diminished atmospheric pressure, one of which was above this "threshold".

MATERIALS AND METHODS

Adult albino mice derived from the same stock were used in both experiments.

Experiment 1

Twenty mice were maintained on a normal diet in four cages. They were exposed to an atmospheric pressure of 425 mm Hg (4570 m) in a decompression chamber and weighed daily (this involved recompression for *ca.* 30 min). When the mean body weight of all animals showed cessation of loss they were removed from the chamber. Daily weighing was continued and when each animal regained its original body weight it was replaced in the chamber at the same atmospheric pressure as before. Since it was considered that variations in the number of animals in the chamber at any one time might affect the degree of weight loss, the first animals to regain their original weights were placed in the chamber with sufficient "blank" non-experimental mice required to bring the total number up to 20; these latter animals were removed from the chamber as more experimental ones regained their original weights. Again, during this second exposure, animals were weighed daily.

Experiment 2

In this experiment three groups of 20 mice, matched so that inter-group differences in mean body weight and variance were minimal, were exposed to pressures of 540 mm Hg (3048 m), 425 mm Hg (4572 m) and 380 mm Hg (6096 m) respectively for 19 days. The daily regimen was the same as that followed in Experiment 1. Daily weighing was continued after the removal of the animals from the chamber.

RESULTS

Experiment 1

Figure 1 shows the changes in mean weight and coefficient variation on the first and second exposures to 425 mm Hg. It is evident that during the first exposure weight is rapidly lost for the first two days, that the rate of loss diminishes after 3 days and that by the fourth day there is a gain in mean weight.

On the second exposure the rate of loss during the first day is similar to that on the first exposure; subsequently the rate is much slower and there is a significant difference is mean weights at the second day ($P < 0.02 > 0.01$). By the fourth day the mean weight is almost identical with that after the fourth day of the first exposure.

It will be seen that changes in the coefficient of variation are small in both exposures, thus indicating that the amount of weight lost by each animal is roughly proportional to its original body weight.

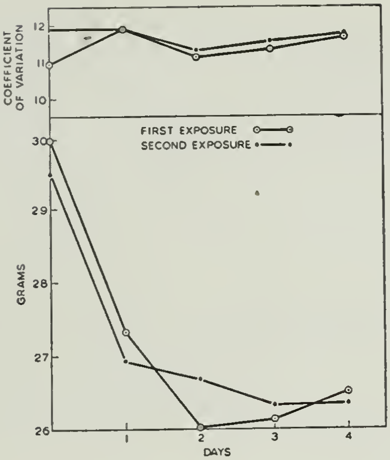

FIG. 1. Changes in body weight and its coefficient of variation during two successive exposures to a simulated altitude of 15,000 ft (4572 m)

Experiment 2

The results of this experiment are shown in Fig. 2. It will be seen that in all three conditions, the weight loss curve is more or less exponential in form. However, whereas an equilibrium level is fairly rapidly reached at the two higher

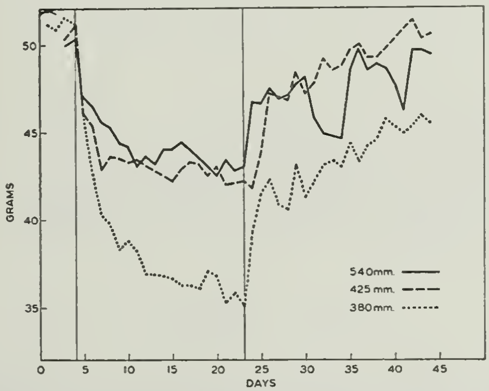

FIG. 2. Changes in body weight during exposure to simulated altitudes of 10,000 ft (3048 m), 15,000 ft (4572 m) and 20,000 ft (6096 m)

pressures, at 380 mm Hg no such equilibrium is achieved during the experimental period. It follows, of course, that the maximum weight loss is not directly linearly related to the atmospheric pressure. So far as rate of loss is concerned, however, it is evident that there is at least some relation to the ultimate equilibrium (or maximum weight loss) level and thus to the pressure itself. It is particularly interesting that, at least during the first 48 hr, the rate of loss at 425 mm Hg is much more similar to the loss at 380 mm Hg than it is to the loss at 540 mm Hg, although in terms of ultimate equilibrium level the similarity is strikingly reversed. It would appear that there is some limit to the amount of weight that can be lost by an animal in a given time. The relative constancy, however, of the coefficient of variation irrespective of the conditions indicates that in each environment the losses in weight of individual animals are proportional to their original body weights.

It may also be noted that in many respects the weight loss curve at 425 mm Hg is to that at 540 mm Hg as the first exposure curve is to the second in the repeated exposures to 425 mm Hg. (Exp. 1). A further point of interest in this experiment is that whereas the animals exposed to pressures of 540 mm Hg and 425 mm Hg regain their original mean body weights after removal from the chamber, those exposed to 380 mm Hg do not.

DISCUSSION

The results of the first experiment clearly indicate that previous experience of lowered atmospheric pressure determines to some extent the effects of subsequent exposure. The nature of the response to the first exposure itself shows that at least part of the weight loss indicates loss of fitness (i.e. the loss which is subsequently regained in reaching the ultimate equilibrium level). At first sight, the difference between this level and the original body weight could represent an adaptive loss. However, the nature of the response to the second exposure, with its reduced rate of loss, suggests that the whole of the weight loss represents an overall loss in fitness. The fact that the final level is the same in each exposure means that the same level of fitness is ultimately reached, which is not surprising.

Whilst it can firmly be concluded that weight changes at simulated high altitudes are indicators of fitness, and can therefore be directly used for estimating the comparative effects of different pressures, it needs to be appreciated that until some sort of equilibrium has been achieved they may not indicate the sequential changes in fitness that are occurring in a group of animals during the period when weight is actually being lost. Fitness obviously is something that can change instantaneously whilst body weight cannot. In other words, there will inevitably be a temporal delay between a particular fitness and the achievement of the corresponding weight: by which time fitness may have changed again. This makes the interpretation of changing rates of weight loss during any one exposure extremely difficult. It is not clear, for instance, whether fitness is at its lowest immediately an animal is placed under conditions of low atmospheric pressure, or whether there is a "carry over" of fitness. It may well be that the effectiveness of at least the initial homeostatic responses is determined by the level of fitness in the habitual environment and that as fitness itself declines, so the capacity to make the appropriate homeostatic responses is lost. One can, however, say from the comparative rates of weight loss at the different pressures, that during the first 24 hr at least, the fitness of the animals under each of these conditions is probably similar; even the animals at 540 mm Hg lose practically as much weight as those at 380 mm Hg. As has been mentioned earlier, the existence of some intrinsic limit to the rate of weight loss might invalidate this conclusion. If, however, rate of loss of weight can be interpreted in terms of fitness, then one must conclude that the effectiveness of the immediate homeostatic mechanisms is the same at all three pressures. It may be added that the fact that there is little or no difference in weight loss between the unacclimatized and pre-acclimatized animals during the first 24 hr at 425 mm Hg implies that pre-acclimatization does not condition the immediate adaptive responses (unlike the long term ones).

So far as the final weight levels are concerned, the interpretation is much more clear cut. It is evident that in all three low pressure environments fitness is diminished as compared with its value at sea level. The fact that an equilibrium weight is achieved at both 540 mm Hg, and 425 mm Hg indicates that adequate homeostasis for survival occurs. It would also appear that there is very little difference in fitness at these two simulated altitudes. At 380 mm Hg, however, the progressive loss in weight suggests that the appropriate homeostatic adjustments cannot be made, and that ultimately there is a progressive loss of fitness. No doubt such a loss itself diminishes the capacity of the animals to achieve homeostasis. The difference between the responses at the lower and two higher pressures indicates that there is probably a clearly defined "threshold pressure" below which permanent adaptation is impossible, and it is of some interest that this must more or less correspond with the acclimatization limit for man (i.e. about 18,000 ft).

Finally, the fact that the animals exposed to 380 mm Hg (in contrast to the others) failed to regain their mean body weight after removal from the experimental environment, not only confirms that these conditions damaged the homeostatic mechanisms, but implies that this damage was permanent and subsequently reduced the fitness of the animals in their habitual environment.

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THE EFFECT OF ALTITUDE ON THE COLD RESPONSES OF LOW ALTITUDE ACCLIMATIZED JATS, HIGH ALTITUDE ACCLIMATIZED JATS AND TIBETANS

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Abstract – The cold responses of six Jat soldiers who had never been exposed to altitude and cold, five Jat soldiers who had had eleven months residence at 12,000–17,000 ft altitude and five Tibetans who were born and raised at altitude were measured for responses against a standard cold exposure of 2° C for 60 min both at high and low altitude. The Tibetans were not measured at low altitude. Both the Jat groups completed the requirements of the standard exposure test at low altitude without difficulty. At 13,000 ft only two of the six low altitude acclimatized subjects completed the standard exposure test while four of the five high altitude acclimatized subjects completed the exposure test at high altitude. All the Tibetans completed the high altitude exposure test. The oxygen consumption of the Jat groups during exposure was higher at high altitude than at low altitude. Both high and low altitude oxygen consumptions of the high altitude acclimatized Jats were lower than those of the low altitude acclimatized Jats. The oxygen consumption of Tibetans was considerably lower than either of those of the Jat groups. As with the oxygen consumptions, a similar pattern was demonstrated for shivering. During cold exposure rectal temperature of both Jat groups was higher at high altitude than at low altitude. Under the conditions of this study it is concluded that altitude induces an augmentation of the acute responses to cold. This is probably due to an impairment of non-shivering thermogenesis resulting in a dependence upon shivering thermogenesis and a decrease in cold tolerance.

Zusammenfassung – Die Reaktionen während eines Standard-Kältetests (60 min bei 2° C) wurden untersucht bei: 6 Jat Soldaten, die nie weder Höhe noch Kälte ausgesetzt waren, 5 Jat Soldaten, die 11 Monate in Höhen von 3700 bis 5200 m gelebt hatten und 5 Tibetanern, einheimisch in grossen Höhen. Die Untersuchungen erfolgten in grosser und niedriger Höhe, bei den Tibetanern nur in grosser Höhe. Beiden Gruppen Jat überstanden den Kältetest in niedriger Höhe ohne Schwierigkeit. In 4000 m Höhe bestanden nur 2 von den nicht höhenangepassten Jats den Test, dagegen 4 von den höhenangepassten. Alle Tibetaner bestanden den Test in grosser Höhe. Der O_2-Umsatz war bei den beiden Jat-Gruppen in grosser Höhe grösser als in niedriger Höhe und der der Tibetaner erheblich unter dem von beiden Jat-Gruppen. Ein ähnliches Ergebnis ergab die Messung des Kältezitterns. Während der Kältebehandlung war die Rektaltemperatur von beiden Jat-Gruppen in grosser Höhe höher als in niedriger Höhe. Aus den Ergebnissen wird der Schluss gezogen, dass Höhe eine Verstärkung der akuten Reaktionen bei Kälteeinwirkung auslöst. Dies ist wahrscheinlich die Folge einer Hemmung der Wärmebildung ohne Zittern, was zu

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einer Abhängigkeit der Wärmebildung durch Kältezittern führt und damit einen Abfall der Kältetoleranz darstellt.

Résumé — On a examiné les réactions de diverses personnes durant une épreuve standard au froid (60 minutes à 2° C). Il s'agissait de 6 soldats Jat qui n'avaient jamais été exposés ni au froid ni à l'altitude, 5 soldats Jat qui avaient séjourné 11 mois entre 3700 et 5200 m d'altitude et 5 Tibétains, indigènes des hautes altitudes. Ils subirent la dite épreuve en altitude et en plaine, les Tibétains toutefois à haute altitude seulement. Les deux groupes de Jats subirent sans difficultés l'épreuve à basse altitude. A 4000 m par contre, 2 seulement d'entre eux qui n'étaient pas acclimatés ont subi l'épreuve avec succès, ainsi que 4 du second groupe. Tous les Tibétains la subirent avec succès. La consommation d'oxygène fut beaucoup plus importante à haute qu'à basse altitude pour les deux groupes de soldats. Les Tibétains en consommèrent par contre beaucoup moins. La mesure des frissons ressentis donne des résultats analogues. Alors qu'ils étaient exposés au froid, les soldats Jat des 2 groupes présentaient des températures rectales plus élevées à haute qu'à basse altitude. On en tire la conclusion que l'altitude augmente la vivacité des réactions déclenchées par le froid. Il s'agit vraisemblablement d'un ralentissement de la production de chaleur sans frissons, ce qui implique une dépendance de la dite production d'un tremblement et, partant, une diminution de la tolérance au froid.

Past studies on the effect of hypoxia on the thermoregulation of man have been carried out in the laboratory (Brown, Vawter and Marburger, 1952; Lim and Luft, 1962). The conclusion drawn from these studies is that temperature regulation is not affected by hypoxia. The present work was carried out to determine whether or not altitude under field conditions affected the temperature regulation of three groups of subjects: a group which was suddenly brought to altitude in a pressurized aeroplane; a group which had been at altitude for 11 months; and a group which was born and reared at altitude. The studies were carried out in Ladakh, India, at 13,000 ft, and at Delhi, India, at an altitude of about 700 ft.

THE SUBJECTS

Six subjects who had never been at altitude were drawn from a Jat regiment of the Indian Army and will be referred to as "low altitude acclimatized Jats." Five subjects who had been at Ladakh for 11 months were drawn from a similar regiment and will be referred to as "high altitude acclimatized Jats". A third group of 5 subjects was obtained locally from a group of Tibetan refugees and will be referred to as "Tibetans". These Tibetans were born at 12 – 13,000 ft and had lived in Ladakh at an average altitude of 14,000 ft for the past 4 years. The term Jat refers to Hindu villagers from the plains area around Delhi.

The average ages and weights of the groups were: Low altitude acclimatized Jats: 21.8 years and 62.9 kg, High Altitude acclimatized Jats: 25.2 years and 57.9 kg, and Tibetans: 25.9 years and 50.1 kg. The Jats at high altitude lived in insulated Mongolian tents heated by a kerosene or diesel-fueled stove. The Tibetans lived in condemned Army canvas tents without heat except for cooking which was usually performed using Yak dung or kerosene as fuel. Ambient temperatures during February and March (the period of study) varied from a minimum of $-20°$ C at night to a maximum of $+5°$ C during sunny days.

METHODS

Oxygen consumption was determined by measuring inspired air with a dry gas meter and analyzing expired gas for O_2 content in a Beckman D_2 oxygen analyzer. Results were corrected to STPD. Skin temperatures were measured in 9 different areas by means of copper-constantan thermocouples and a Brown potentiometer. Rectal temperatures were measured with a thermistor connected to a Yellow Springs Instrument Company portable telethermometer. Shivering was measured by using a portable integrating Offner EEG/EMG type T machine, with the electrodes placed on the anterior aspect of the thighs at the junction of the upper and middle third. These measurements were made in response to a standard cold exposure test of 2° C air temperature for 60 min with subjects dressed only in shorts and reclining on a stretcher. The subjects were fasted for 18–24 hr and responses to thermoneutral conditions were measured for 30 min just prior to removal to the cold. Test temperatures at sea level were obtained in a cold chamber and, at altitude, in a tent cooled by the outside ambient temperature. Mean cold test temperatures obtained at sea level were $1.5 \pm 0.5°$ C for the low altitude acclimatized Jats, and $2.2 \pm 0.7°$ C for the high altitude acclimatized Jats. At altitude, these were $3.4 \pm 1.1°$ C for the low altitude acclimatized Jats, $2.3 \pm 0.9°$ C for the high altitude acclimatized Jats, and $1.8 \pm 0.8°$ C for the Tibetans. The Tibetans could not be measured at sea level. T-tests on intra-group results were performed on a paired data basis, and on a non-paired basis when results were used to compare one group against another. Statistical significance was set at the 5 per cent level of confidence.

RESULTS

The low altitude acclimatized Jats completed the sea level cold exposure test without complaint or problems. However, at altitude, only 2 of the 6 subjects completed the test with strong complaints of pain in the lower extremities. Of the 4 subjects who did not complete the altitude cold exposure test, two failed because of muscle cramps associated with hyperventilation, and 2 failed because of unbearable pain in the lower extremities. All failures in this group occured at 35 min of exposure. Two of the 5 high altitude acclimatized subjects failed at 45 min of exposure because of unbearable pain in the lower extremities. All the subjects in both groups complained of greater subjective discomfort during the standard cold test at altitude than at sea level. The pain in the lower extremities was not related to surface temperatures which were not lower than those observed at sea level, suggesting that altitude may have decreased the cold pain threshold.

Figure 1 illustrates the changes in oxygen consumption. All zero time values in all figures represent those obtained under basal thermoneutral conditions. Basal metabolic rates in the Jat groups were unchanged by altitude; indeed, there were

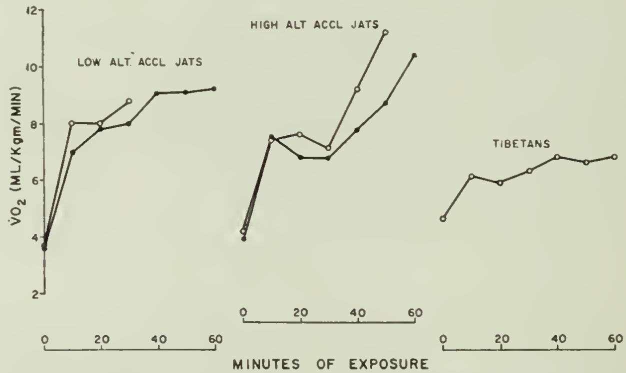

FIG. 1. Oxygen consumptions obtained during a standard cold exposure at sea level (closed circles) and at altitude (open circles)

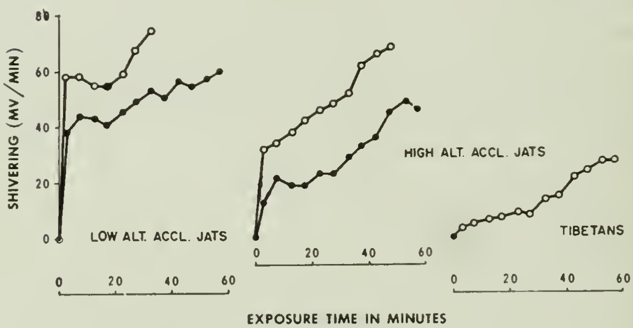

FIG. 2. The electrical activity of shivering obtained during cold exposure at sea level (closed circles) and at altitude (open circles)

no differences between the basal metabolic rates of three groups under all conditions of measurement. In both Jat groups, metabolism in the cold was not affected by altitude. Oxygen consumption of these two groups did not differ from each other under all conditions of measurement. On the other hand, the Tibetans had a substantially lower oxygen consumption in the cold than the Jat groups ($p<0.01$).

Figure 2 illustrates the shivering response during cold exposure. Shivering in both Jat groups was increased by altitude ($p < 0.05$). Because of high variability, no intergroup differences could be demonstrated statistically in both environments. The Tibetans had a substantially lower shivering rate than either of the Jat groups ($p < 0.01$).

Fig. 3 shows the influence of altitude on the skin temperature threshold of shivering. In both Jat groups altitude produced a shift to the right indicating that altitude decreased the skin temperature threshold of shivering. An even greater

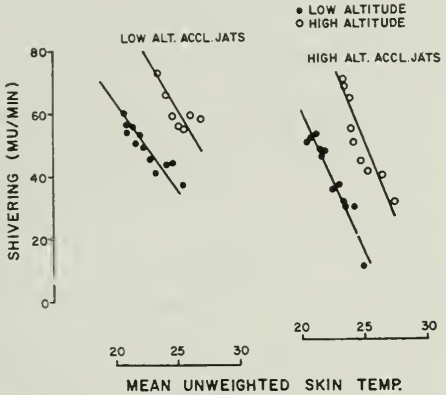

FIG. 3. The relationship between mean unweighted skin temperature and shivering obtained in the Jat groups at sea level (closed circles) and at altitude (open circles)

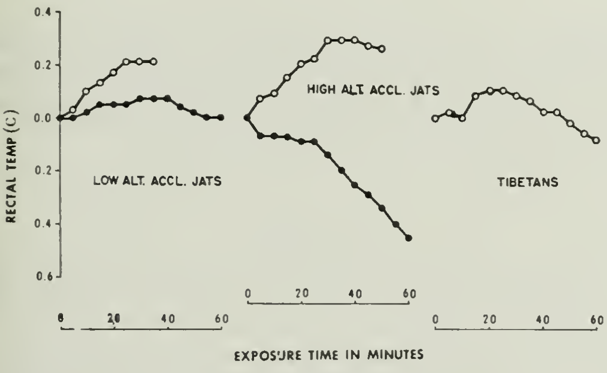

Fig. 4. The relative change of rectal temperature during cold exposure at sea level (closed circles) and at altitude (open circles)

shift can be demonstrated for the relationship between shivering and rectal temperature but this relationship is not considered functional under the conditions of this experiment.

Fig. 4 shows the relative changes in rectal temperature. Rectal temperatures obtained under basal conditions were not influenced by altitude. During cold exposure, both groups had elevated rectal temperatures at altitude ($p < 0.01$). At sea level, the rectal temperature of the high altitude acclimatized Jats decreased whereas that of the low altitude acclimatized Jats remained stable ($p < 0.01$). Cold exposure at altitude produced no significant differences in rectal temperature in the three groups.

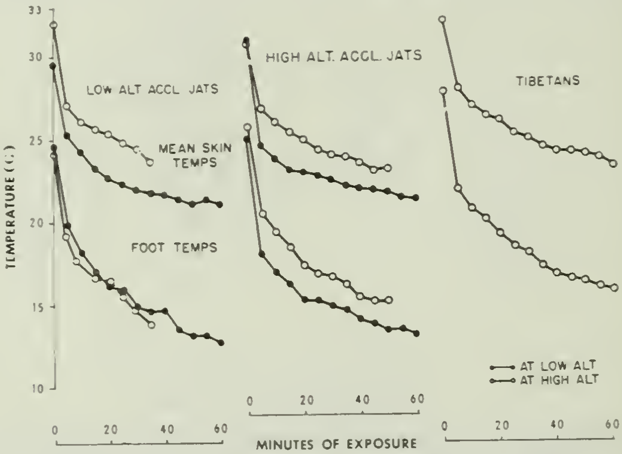

Fig. 5. Skin temperature changes during cold exposure at sea level (closed circles) and at altitude (open circles)

Mean unweighted skin temperatures and foot temperatures measured on the dorsum of the foot are shown in Fig. 5. Although there was a tendency for skin temperatures to be higher at altitude, no statistically significant differences could be demonstrated within each group or between groups.

DISCUSSION

In these experiments, altitude had an adverse effect on cold tolerance as indicated by inability to withstand the standard cold exposure test for the 60-min requirement. However, this decreased tolerance could not be accounted for by the observed values of oxygen consumption or of thermal balance as measured by rectal and skin temperatures. These findings are similar to those of Brown, Vawter and Marburger (1952) who reported that measured responses of humans to cold does not appear to be altered by reduced PO_2, this is contrary to opinions expressed by flying personnel on a subjective basis. In this study the determinations of shivering and rectal temperature were the only measurements which showed consistent changes as a result of altitude. A decrease in shivering, rectal temperature, and oxygen consumption during cold exposure has been interpreted previously as indicating cold acclimatization in man (Davis, 1961; Davis, Johnston and Bell, 1961). Of these, only the decrease in shivering when it has been measured, has proved to be the most consistent (Davis, 1961; Joy, Poe and Davis, 1962). A rectal temperature decrease appears to be a relatively early change in the process of acclimatization to cold (Davis, Johnston and Bell, 1961). The lower rectal temperatures in the high altitude acclimatized Jats measured at sea level suggested that they had achieved some measure of cold acclimatization. Due to high variability, no differences could be demonstrated for shivering in these two groups, although mean levels were much lower in the high altitude acclimatized Jats. Since shivering increased without a comparable increase in oxygen consumption, it would appear that altitude may have impaired non-shivering thermogenesis (Davis, 1963). Therefore it may be suggested that altitude impairs certain (as yet undetermined) mechanisms of cold acclimatization resulting in greater discomfort and lower tolerance during cold exposure regardless of total heat production and thermal balance. At altitude, the Tibetans had a significantly lower shivering rate, a lower cold-induced oxygen consumption, and a greater tolerance to cold than either of the Jat groups, presumably reflecting a greater degree of cold acclimatization in this group. By the same token, the high altitude acclimatized Jats showed some degree of cold acclimatization although it was much less than that of the Tibetans. In Ladakh, over-protection from and avoidance of cold by those alien to the area was in evidence and may account for their lowered cold tolerance in keeping with the previously reported finding that living in a cold climate with adequate protection does not insure the acquisition of cold acclimatization (Joy, Poe and Davis, 1962). Although total heat production in the cold was unchanged by altitude, rectal temperature was nevertheless higher at altitude than at sea level. Since skin temperatures were not different, these subjects at altitude were in a higher thermal balance. Although this may be related to the impairment of cold acclimatization mechanisms, it also could have been consequent to the lowered convective heat transfer coefficient of ambient air at altitude which in this study was reduced by a factor of 0.21 (McAdams). In spite of this decrease in convective heat transfer, cold sensitivity and shivering were greatly increased without a change in total heat production, further suggesting that an impairment of the non-shivering fraction of the thermoregulatory mechanism had occurred at altitude.

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PULMONARY HYPERTENSION IN NORMAL MAN RESIDING AT 10,000 FEET

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Abstract – In over 500 people 12 to 18 years old living permanently at 10,150 ft, the presence of pulmonary hypertension was sought by physical examination, electrocardiography, and chest *X*-ray. The average mean QRS axis was +84° compared with +59° at sea level. This right axis deviation suggested mild pulmonary hypertension. Cardiac catheterization in 28 normal individuals revealed average mean pulmonary arterial pressures elevated to 25 mm Hg at rest, and rising to 54 mm Hg during exercise. This hypertension results from pulmonary vascular resistance increased by chronic hypoxia, and not from polycythemia or high cardiac output. These "second generation" natives of high altitude have higher pulmonary arterial pressures than the Indians in the Peruvian Andes.

Zusammenfassung – Über 500 Personen im Alter von 12–18 Jahren, die dauernd in der Höhe von 3100 m leben, wurden auf pulmonale Hypertonie physikalisch und elektrokardiographisch untersucht und durchleuchtet. Die durchschnittliche mittlere QRS-Achse war +84° verglichen mit +59° auf Seehöhe. Diese Rechts-Achsenabweichung deutet auf pulmonale Hypertonie leichten Grades hin. Herzkatheterisierung bei 28 normalen Personen zeigte einen durchschnittlichen mittleren pulmonalen arteriellen Druck, der auf 25 mm Hg in Ruhe und 54 mm Hg während der Arbeit erhöht war. Dieser Hochdruck ist Folge des höheren Pulmonalgefässwiderstandes bei chronischer Hypoxie und ist unabhängig von der Polycythämie oder grossem Herzminutenvolumen. Diese in 2. Generation in der Höhe Einheimischen haben einen höheren Pulmonalarteriendruck als Indianer in den peruanischen Anden.

Résumé – Plus de 500 personnes âgées de 12 à 18 ans et vivant en permanence à plus de 3100 m d'altitude ont été soumises à un examen radioscopique, physique et électrocardiographique afin de déceler une hypertonie pulmonaire éventuelle. L'axe QRS moyen était de 84° alors qu'il est de 59° au niveau de la mer. Ce décalage de l'axe vers la droite indique une légère hypertonie pulmonaire. Un cathétérisme cardiaque effectué sur 28 sujets en pleine santé a montré que la pression artérielle pulmonaire moyenne était plus élevée en moyenne de 25 mm Hg au repos, de 54 mm Hg au travail. Cette pression élevée est le résultat de la résistance accrue des vaisseaux pulmonaires par hypoxémie chronique et dépend de la polycythémie ou dilatation du coeur. Les «indigènes de deuxième génération» à haute altitude ont une pression artérielle pulmonaire plus élevée que les Indios des Andes péruviennes.

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THE complex process of acclimatization to high altitude has interested men for a great many years. Observations of acute changes in physiology have been made on numerous mountaineering expeditions. Unquestionably the most ambitious endeavor of this type was the establishment of a semi-permanent laboratory at 19,000 ft by Griffith Pugh during the 1960–61 Himalayan Expedition (Pugh *et al.*, 1964). Here, the cardiopulmonary adjustments to life at extreme altitude were studied over several months in a group of men from sea level.

The acclimatized state of the new-comer to high altitude differs somewhat from the physiology of the permanent resident at altitude. Investigations of such lifelong acclimatization have been actively conducted in the Peruvian Andes for many years. Hurtado has added much to our knowledge of respiratory adaptation. More recently, Peñaloza has demonstrated some of the remarkable circulatory modifications which exist in those natives (Peñaloza *et al.*, 1963).

We have, then, two extremes in acclimatization. On the one hand is the man from sea level who moves to high altitude. At the other extreme is that vast population in the Andes which has lived permanently at altitudes above 12,000 ft for generations. There lies between these two extremes a third group which broadens still further the spectrum of acclimatization. This third group consists of individuals born and living at high altitude, whose parents came from low altitude. These "second generation" natives are truly a distinct group, and will be the subject of this presentation.

In North America, there are many high mountain peaks ranging from 18,000 ft in Mexico to 20,000 ft in Alaska. Within the state of Colorado, there are more than 50 peaks above 14,000 ft. However, relatively few people live at truly high altitudes. The highest community in North America is located at only 10,150 ft (3100 m).

This is the city of Leadville, Colorado, with a population of 7000 located in the Rocky Mountains 100 miles west of our Medical Center in Denver. Leadville was first settled a little over 100 years ago by miners seeking gold and silver. It is still basically a mining town, but today the valuable metals are molybdenum and tungsten. The oldest families in the city came four generations ago, but most families moved there in the last 50 years. Their children are the "second generation" natives whom we studied.

I personally have been interested in the pulmonary circulation for a number of years. In 1960, I investigated the development of severe pulmonary hypertension in normal cattle taken to high altitude (Grover *et al.*, 1963). Two years ago, when I had the privilege of talking with Dr. Peñaloza in Lima, I was naturally intrigued by his finding of marked pulmonary hypertension in normal man living at 15,000 ft. No such elevation of pulmonary arterial pressure exists, in Denver at 5300 ft, or even in Mexico City at 7300 ft (DeMicheli *et al.*, 1960). Therefore, at what altitude does this phenomenon begin? Would there be detectable evidence of pulmonary hypertension in man living at 10,000 ft? To find out, we organized the following survey in Leadville.

Virtually everyone in the adolescent age group living in Leadville is attending school. This makes them a convenient group for study. We elected to examine the 508 students between the ages of 12 and 17 years. On each individual, we obtained a medical history, a physical examination by a trained cardiologist, an electrocardiogram, and a chest X-ray. This proved to be an extensive undertaking, and was successful thanks to the skilful organization of Dr. Walt Weaver. We found 14 cases of organic heart disease, and these were excluded from further evaluation.

Most of the remaining normal healthy students had some clinical evidence of pulmonary hypertension. On auscultation, the sound of pulmonic valve closure was frequently of increased intensity. The major branches of the pulmonary artery were increased in size on many chest X-rays. Most consistent was the presence of right axis deviation on the electrocardiogram. The average mean QRS axis (Å QRS) was $+84°$ compared with $+59°$ at sea level. Further comparisons are made in Table 1.

Table 1. Increase in right axis deviation with decrease in alveolar oxygen tension

Community	Altitude ft	P_{AO_2} mm Hg	ÅQRS
Lima, Peru	500	104	59°
Denver, Colorado	5,300	81	69°
Leadville, Colorado	10,150	65	84°
Morococha, Peru	14,900	50	125°

The degree of elevation in pulmonary arterial pressure which these clinical observations implied could only be determined by direct measurement using a cardiac catheter. For this further investigation, we selected 28 individuals who were representative of the whole group in the survey. Using the electrocardiogram as one criterion, the average Å QRS for the 28 catheterized subjects and the nearly 500 students examined were $+96°$ and $+84°$, respectively.

The catheterization studies were performed in the Radiology Department of the modern Leadville hospital. Pressures, blood gases, cardiac output, and ventilation were obtained on each subject at rest and during supine bicycle exercise. In Leadville, the ambient PO_2 is 110 mm Hg. To evaluate the role of this degree of hypoxia, the inspired PO_2 was raised to 220 mm Hg during exercise. Further, the inspired PO_2 was lowered to 70 mm Hg at rest.

None of the subjects had any evidence of valvular obstruction. Furthermore, there was no evidence of any intracardiac shunt using the sensitive hydrogen-platinum technique. The normality of every subject was thereby further documented At rest, nearly every subject had a modest elevation of his mean pulmonary arterial (PA) pressure. The average for the group was 25 mm Hg, compared with 12 mm Hg at sea level. Six subjects had resting mean PA pressures less than 20 mm Hg, while 4 had pressures higher than 30 mm Hg (Fig. 1).

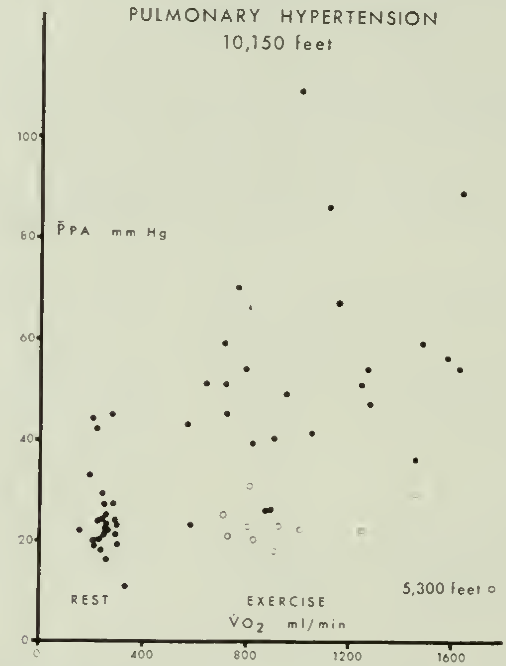

FIG. 1. Mean pulmonary arterial pressure ($\overline{P}$ PA) in supine subjects at rest and during leg exercise. The severity of exercise is indicated by the level of oxygen uptake ($\dot{V}O_2$). Ten normal subjects studied at lower altitude (open circles) are included for comparison. Pulmonary hypertension of mild degree is present at rest, and becomes moderate to severe during exercise in normal subjects at high altitude

The most impressive finding at catheterization was the remarkable rise in PA pressure during vigorous supine exercise (Fig. 1). Recall that at lower altitudes, the mean PA pressure seldom exceeds 30 mm Hg during exercise. In contrast, all but 5 of these Leadville students had mean PA pressures greater than 40, and the average for the group was 54 mm Hg. Seven exceeded 65 mm Hg. The highest pressure we saw was in a 15-year-old girl who was the skiing champion of her high school. During exercise, her PA pressure was 165/90, or a mean of 109 mm Hg. She is totally asymptomatic, and by all other criteria perfectly normal.

What is the basis for this pulmonary hypertension? First, we examined cardiac output, knowing that output is increased by acute hypoxia. In these residents at high altitude, however, the cardiac output was no different from what we see in normals (Fig. 2). The same relationship exists between oxygen uptake and cardiac output at Leadville as at lower altitudes (Denver). Pugh found that this relationship is maintained even at 19,000 ft. Hence. a high output state does not exist in these subjects.

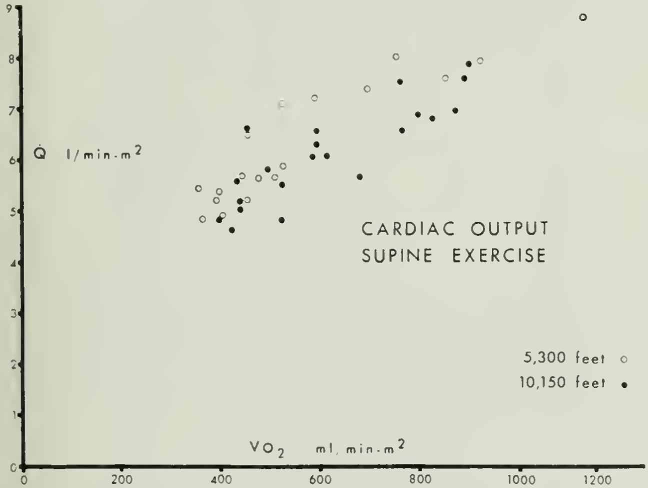

FIG. 2. Cardiac output ($\dot{Q}$) at various levels of oxygen uptake ($\dot{V}O_2$) during supine exercise in normal subjects at high altitude (solid dots) and at lower altitude (open circles). There is no significant difference between the two groups

In addition the pulmonary arterial wedge pressure was normal. Hence, the pulmonary hypertension was not a passive reflection of some rise in pulmonary post-capillary pressure as in mitral stenosis.

Next, we examined the relationships between pressure and flow, i.e. pulmonary vascular resistance (Fig. 3). At low altitudes, the resting pulmonary resistance per square meter of body surface area is less than 400, and generally decreases during exercise. By contrast, in the Leadville subjects the resting resistance was usually greater than 400, and with exercise remained unchanged, or actually increased, but rarely decreased. Here, then, is one of the basic differences between the native of high altitude and the native of low altitude in terms of vascular adjustment.

An increase in calculated pulmonary vascular resistance could be produced by polycythemia and an increase in blood viscosity. However, the average hematocrit in our young Leadville subjects was only 46 per cent, which is virtually normal. This could not account for the observed increase in resistance or the elevated pulmonary arterial pressures.

That hypoxia can produce pulmonary vasoconstriction has been well established (Fishman, 1962). Hence, the chronic hypoxia of high altitude might be expected to increase vascular resistance in the lung by this mechanism. Just how hypoxic were the subjects studied in Leadville? Figure 4 illustrates the relationship bet-

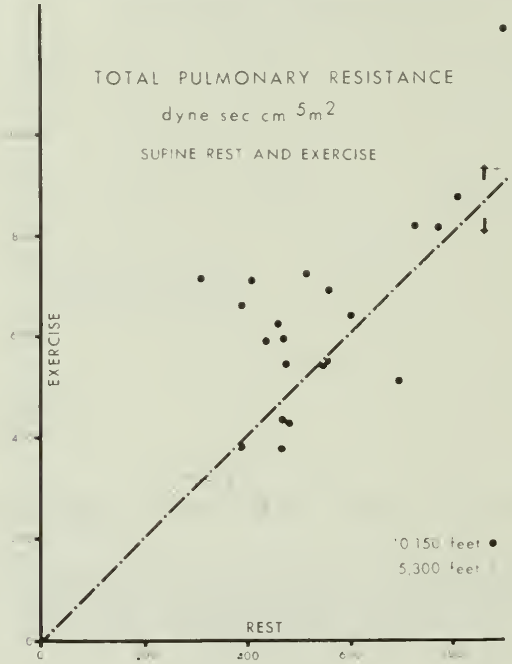

FIG. 3. Total pulmonary resistance during supine exercise compared with resting values in normal subjects at high altitude (solid dots). Ten normal subjects at lower altitude (open circles) are included for comparison. The total resistance at rest is greater at high altitude, and often increases further during exercise

ween ventilation, which largely determines alveolar oxygen tension, and the resulting arterial oxygen saturation. Examination of the minute ventilation ($\dot{V}$, BTPS) per liter of oxygen uptake ($\dot{V}O_2$, STPD) reveals definite hyperventilation at rest, with relatively high arterial saturations as a consequence (average 92 per cent). During exercise, hyperventilation was less marked, and arterial saturations fell an average of 5 per cent. In other words, these subjects were more hypoxic when exercising than at rest. To an extent, however, this is artifact. It is probable that the hyperventilation measured under our experimental conditions reflects apprehension in these unsedated young students. In their everyday lives, they undoubtedly hyperventilate less at rest than our data would indicate.

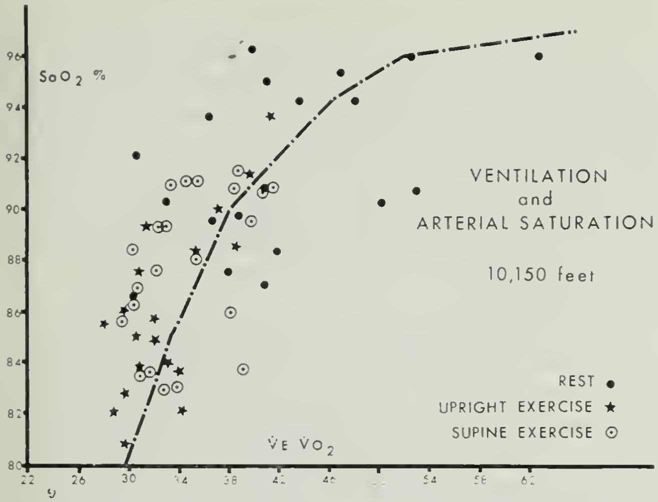

FIG. 4. Arterial blood oxygen saturation (SaO_2) related to minute ventilation ($\dot{V}E$, BTPS) per liter of oxygen uptake ($\dot{V}O_2$, STPD). Since ventilation determines alveolar oxygen tension, the resulting hemoglobin-oxygen dissociation curve has been indicated by the broken line. During exercise, ventilation relation to oxygen uptake decreases, with a resulting fall in arterial saturation

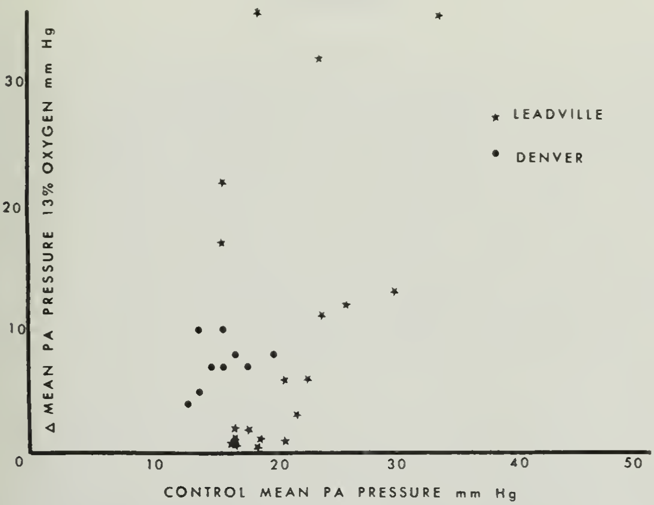

FIG. 5. Pulmonary arterial pressure response to acute hypoxia. The change in mean pulmonary arterial pressure during hypoxia is related to the mean pressure at rest. In subjects at lower altitude, the average increase in pressure was 10 mm Hg. Among subjects at high altitude (stars), some had a much greater pressure rise (hyper-reactors) while others had virtually no change at all (hypo-reactors)

It was important to determine the response of these individuals to hypoxia. Since they were so minimally hypoxic at rest, we induced further hypoxia with a gas mixture having an inspired oxygen tension of 70 mm Hg. The results were unexpected (Fig. 5). The exaggerated rise in PA pressure in some subjects (hyper-reactors) might have been anticipated. However, we were surprised to find a sizable group who had virtually no increase in PA pressure (hypo-reactors) – a response actually less than we see at lower altitude. Further analysis revealed that in general, those individuals who had the greatest rise in PA pressure with hypoxia at rest were the same individuals who developed the most marked pulmonary hypertension during exercise.

Since arterial saturation fell during exercise, to what extent was this added hypoxia responsible for the rise in PA pressure? To answer this question, we administered oxygen during exercise to remove the hypoxic stimulus. The effect of breathing 41 per cent oxygen was prompt and dramatic, producing a fall in mean PA pressure in every case, the average decrease being 20 mm Hg. Oxygen also decreases the cardiac output with exercise. However, the pressure fall was much greater than the decrease in output, i.e. the pulmonary vascular resistance was indeed lowered. During exercise, removal of hypoxia reduced the resistance to blood flow through the lung, presumably by relieving pulmonary vasoconstriction.

DISCUSSION

At an altitude of 10,150 ft, we documented the existence of pulmonary hypertension, which in many individuals became remarkably severe during exercise, in perfectly normal healthy young high school students. How do these findings compare with observations made nearly 5,000 ft higher at Morococha in the Andes (Peñaloza *et al.*, 1962)? To begin with, the hypoxic stimulus is more severe in Morococha. The average resting arterial saturation is reduced to 78 per cent, and falls further during exercise to 69 per cent. In spite of this, mean PA pressures are only 5 mm Hg higher than ours, even during exercise. When you consider that in the subjects at Morococha, the average hematocrit was increased to 59 per cent, there was probably a significant increase in blood viscosity contributing to the pulmonary hypertension. In fact, calculations by Roos (1962) suggest that the increased blood viscosity alone could adequately explain all of the elevation in PA pressure, without invoking any pulmonary vasoconstriction. This is in contrast to the normal hematocrit of 46 per cent found in our subjects.

More recently, Hultgren has reported hemodynamic measurements made at La Oroya (12,300 ft) in Peru. He found PA pressures actually lower than ours, even during exercise. Furthermore, his subjects were also polycythemic. Electrocardiographic studies obtained by Peñaloza in Huancayo at 10,900 ft indicate less right axis deviation than at La Oroya, and much less than at Morococha. From this, we would predict that when PA pressures are measured in Peruvian natives living at an altitude comparable to Leadville, there will be found much less pulmonary hypertension than we observed.

What does this mean in terms of acclimatization to high altitude? What is the basis for this difference in the regulation of the pulmonary circulation? One could question the importance of race: our subjects were Caucasian; in the Andes they were native Indian (Quechua). However, I think genetic background is probably a more significant variable. The Peruvian natives have lived at extreme altitudes for at least 20 generations, whereas our subjects are only "second generation" natives. Over long periods of time, a process of natural selection could operate to favor the hypo-reactors, leading eventually to a population with more modest pulmonary hypertension when hypoxic. There is good evidence that this occurs in herds of cattle raised at high altitude (Hultgren and Miller, 1961).

Our subjects presented a very wide range of PA pressures when stressed with either exercise or hypoxia. The recognition of this wide range of pulmonary vasomotor reactivity is in itself important (Grover *et al.*, 1963). This phenomenon would not be apparent at sea level, but only in an environment of chronic hypoxia. In response to this stimulus, the hyper-reactors have the opportunity to distinguish themselves. One reflection of this is the wide range in the mean QRS axis at high altitude compared with the narrow range at sea level. Within limits, some degree of pulmonary hypertension at high altitude is certainly not detrimental. However, excessive hypertension may well represent an adverse form of acclimatization.

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ÜBER DIE BERGKRANKHEIT

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Abstract – All signs and symptoms of disease produced by high altitude or in the low pressure chamber are collectively termed "Mountain sickness". A list of all signs and symptoms from the literature and the author's own observations make it possible to differentiate between high altitude insufficiency, true mountain sickness, and Monge disease. These three kinds of high altitude disease including lung edema at latitude can be referred to certain phases of acclimatization to high altitude. The pathogenesis which is still partly unknown is discussed and therapeutic measures are mentioned.

Zusammenfassung – Alle durch die Höhe und auch durch Sauerstoffmangel in der Unterdruckkammer hervorgerufenen Beschwerden und Krankheitserscheinungen werden allgemein als „Bergkrankheit" bezeichnet. Eine Zusammenstellung der klinischen Symptomatik aus der Literatur und nach eigenen Beobachtungen macht eine Unterscheidung in akute Höheninsuffizienz, echte Bergkrankheit und Monge'sche Krankheit möglich. Alle drei Formen der Höhenkrankheit lassen sich einschliesslich des Lungenödems der Höhe pathophysiologisch bestimmten Phasen der Höhenakklimatisation zuordnen. Die teilweise noch ungeklärte Pathogenese wird erörtert und die Therapie kurz besprochen.

Résumé – Tous les maux et maladies provoqués par l'altitude ou par le manque d'oxygène au caisson sont en général dénommés « mal de montagne ». La compilation des symptômes cliniques décrits dans la litérature appuyés en outre par des observations personnelles permet une discrimination entre les insuffisances aigües dues à l'altitude et la maladie de Monge. Les trois formes du mal de montagne de même que l'oedème pulmonaire d'altitude peuvent être rangées dans les différentes phases patho-physiologiques de l'acclimatation à l'altitude. On indique brièvement les pathogénèses qui ne sont encore que particllement expliquées et on en discute la thérapie.

ALLE Krankheitserscheinungen, die durch die Höhe ausgelöst werden, bezeichnet man üblicherweise als „Bergkrankheit". Selbst die im isolierten Sauerstoffmangel, z. B. in der Unterdruckkammer beobachteten Störungen werden unter diesem Begriff diskutiert. Eine Durchsicht der Literatur läßt jedoch erkennen, daß sich hinter der „Bergkrankheit" ganz verschiedenartige klinische Symptome und Syndrome verbergen.

1925 trennte Monge ein charakteristisches Syndrom von dem Sammelbegriff der Bergkrankheit ab: Extreme Vermehrung der Erythrozyten und des Hämoglobins, Emphysem, Hyperthrophie des rechten Ventrikels, Zunahme des Drucks in der Arteria pulmonalis (Rotta *et al.*, 1956), subjektiv ausgezeichnet durch Müdigkeit, Kopfschmerzen und z. T. psychische Störungen (Monge, 1939). Da diese Krankheit erst nach monate- oder jahrelangem Höhenaufenthalt auch bei Höhenbewohnern auftritt, wurde sie als „chronische Bergkrankheit“, später als Monge'sche Krankheit bezeichnet.

Die vielfältigen Untersuchungen der letzten Jahrzehnte über den Einfluß des Höhenwechsels auf den Organismus lassen nun auch einen Vergleich mit den verschiedenen Erscheinungsbildern der sogenannten akuten Bergkrankheit zu und ermöglichen eine weitere Differenzierung.

Unmittelbar während der Fahrt in die Höhe und kurz nach der Ankunft besteht eine Bradykardie, eine Verkleinerung des Herzminutenvolumens und eine leichte Blutdruckabnahme (Durig, 1911; Haus u. Jungmann, 1954). Oberhalb 3000 m treten Symptome des akuten Sauerstoffmangels hinzu: Müdigkeit, Gähnen, Vergeßlichkeit und Schwindelgefühl. In dieser Phase kann es zum Kollaps kommen. Sauerstoffatmung beseitigt die Störungen meist schnell.

Die Ursache ist nicht allein im Sauerstoffmangel zu suchen. Im Unterdruckversuch ließ sich bisher keine Bradykardie und Minutenvolumenverkleinerung erzeugen. Auch tritt der Kollaps erst in größeren Nennhöhen auf, ihm geht eine deutliche Zyanose, Pulsbeschleunigung und oft eine Euphorie voraus. Andererseits werden solche Kollapserscheinungen in den Bergen schon in Höhen von nur 2000 m gelegentlich beobachtet. Das klinische Bild ergibt sich aus einer Mischung von echten O_2-Mangelsymptomen und einer unspezifischen Reaktion des vegetativen Systems im Sinne von Hoff (1952) und von Selye (1950), die besonders bei vegetativ labilen Personen deutlich wird. Dieses Krankheitsbild ist grundsätzlich von der echten „Bergkrankheit“ zu unterscheiden und sollte besser als *akute Höheninsuffizienz* bezeichnet werden.

Nach 1–6 Stunden Höhenaufenthalt entwickelt sich eine zweite Phase der Höhenreaktion mit Tachycardie (Grandjean, 1944), Zunahme des Herzminutenvolumens (Haus und Jungmann, 1954), leichter Blutdruckerhöhung (Durig, 1911), in Höhen über 3000 m verbunden mit Hyperventilation, Schwächegefühl, Schlaflosigkeit und Cheyne-Stokes'scher Atmung (Grandjean, 1944). In 2000 m Höhe beginnt diese Phase 1–2 Stunden nach der Ankunft (Haus u. Jungmann 1954), in 4600 m war die Tachykardie 4 Stunden nach der Ankunft, d. h. 8 Stunden nach Beginn des Höhenwechsels ausgeprägt (Hurtado u. Jungmann, 1961), in den Untersuchungen von Peñaloza (1961) u. Mitarb. sogar erst 12 Stunden nach der Ankunft in 4600 m Höhe. Diese Phase dauert bis zu 8 Tagen.

Aus dieser zweiten Phase der Höhenreaktion entwickelt sich die echte „Bergkrankheit“, in Südamerika „Soroche“ genannt mit einer typischen Latenz von Stunden bis Tagen (Durig, 1911; Holmquist, 1934; Keys, 1938; Delius, Opitz u. Schoedel, 1942). Holmquist beschrieb 1934 6 Fälle in 3500 m Höhe, bei denen die Latenz 1–15 Stunden betrug. In den Untersuchungen von Delius, Opitz u. Schoedel in 4500 m Höhe traten Symptome der Bergkrankheit erst nach mehreren Tagen auf. Der häufigste Zeitpunkt der Manifestation ist der Morgen nach der ersten Höhennacht.

Schon diese Latenz macht den Sauerstoffmangel als direkte Ursache unwahrscheinlich. Aber auch die Symptomatik entspricht nicht den Beobachtungen aus der Unterdruckkammer. Subjektiv bestehen: starke Kopfschmerzen, Übelkeit, Erbrechen, Schwindelgefühl; objektiv: Blässe, Tachykardie (z. T. auch Bradykardie), etwas erhöhter Blutdruck mit kleiner Blutdruckamplitude, kleines Herzminutenvolumen, ein hoher Tonus des Arteriensystems sowie eine leicht erhöhte Körpertemperatur. Holmquist fand 1934 einen erhöhten Blutzuckerspiegel und einen erniedrigten Calziumspiegel im Serum. Auffallend sind dabei: die Erhöhung

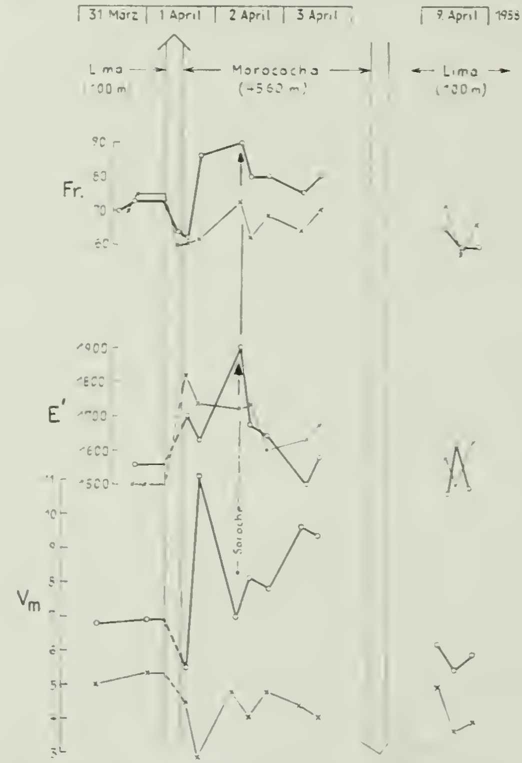

ABB. 1. Pulsfrequenz (Fr.), Tonus des Arteriensystems (E'), berechnet aus Pulswellengeschwindigkeit und der Eigenschwingung des Arteriensystems sowie Herzminutenvolumen (Vm) beim Übergang in 4560 m Höhe.
o——o Meßwerte einer gesunden, nicht höhengewohnten Person, die am 2. April morgens ausgeprägte Symptome der Bergkrankheit zeigte;
×——× Meßwerte eines in 3500 m Höhe geborenen Einwohners, der subjektiv nur geringe Beschwerden in der Höhe empfand

der Körpertemperatur (Durig, 1911; Holmquist, 1934; Hurtado u. Jungmann, 1962), die Verkleinerung des Herzminutenvolumens (Delius u. Mitarb. 1942; Grollmann 1930; Hurtado u. Jungmann 1961) und die Blässe der Haut ohne wesentliche Zyanose. Auch Kopfschmerzen und Übelkeit sind viel intensiver als im reinen Sauerstoffmangel in gleicher Nennhöhe. Dill fand 1938 keinen Zusammenhang zwischen dem Sauerstoffgehalt der Arterien und den Erscheinungen der Bergkrankheit.

Das typische Krankheitsbild ließ sich in der Unterdruckkammer bisher überhaupt nicht erzeugen. Selbst in den 4 Wochen dauernden Sauerstoffmangelversuchen der sog. „Operation Everest“ in Nennhöhen bis 9000 m wurde keine echte Bergkrankheit ausgelöst (Houston, 1946). Dill beschrieb 1938 einen Fall mit vergleichbarer Symptomatik, der nach einem 6-stündigen O_2-Mangelversuch in Meereshöhe auftrat und 24 Stunden anhielt trotz zusätzlicher Sauerstoffatmung.

Die Symptome verschwinden bei Sauerstoffatmung nicht sofort. Therapeutisch und prophylaktisch haben sich vielmehr Salicylsäure -und Diaminophenazon-Präparate bewährt, die keinen Einfluß auf die Sauerstoffversorgung haben.

Tabelle 1. Symptome der Bergkrankheiten

	Akute Höheninsuffizienz	Akute Bergkrankheit	Chronische Bergkrankheit
Zeitpunkt der Manifestation	sofort	nach Stunden bis Tagen	nach Monaten bis Jahren
Beschwerden	Müdigkeit Gähnen Schwäche Vergeßlichkeit Übelkeit	Kopfschmerzen Übelkeit Erbrechen Schwindel Dyspnoe	Kopfschmerzen Dyspnoe Schwäche cerebrale Störungen
Symptome	(Cyanose) Bradykardie Hypotonie	Blässe Tachykardie Kleine Blutdruckamplitude erhöhter Arterientonus Atmung erhöhte Körpertemperatur	Cyanose Bradykardie Hypotonie extreme Polyglobulie Sensibilitätsstörungen
Komplikationen	Kollaps	Hyperemesis Lungenödem	Emphysem Cor pulmonale

Insgesamt weisen sowohl das klinische Bild als auch die empirisch erprobte Therapie auf eine *Intoxikation* hin. Der Sauerstoffmangel ist ursächlich mit Sicherheit beteiligt, da die Bergkrankheit nicht unterhalb von 2500 m beobachtet wird. Eine Hypothese würde sowohl die Latenz, das klinische Bild als auch die therapeutischen Erfahrungen erklären: eine Intoxikation mit unvollständig oxydierten Produkten des intermediären Stoffwechsels. Nach Reed u. Kellogg (1958) ist die arterielle Sauerstoffspannung im Schlaf auch in 4300 m Höhe sehr niedrig. Deshalb kommt es am Morgen zu besonders starken Beschwerden. Allerdings wurden bisher solche Stoffwechselstörungen bei der Bergkrankheit noch nicht nachgewiesen, wahrscheinlich auch noch nicht gesucht. Eine andere Hypothese nimmt ein Hirnödem an, doch fehlen Beobachtungen über eine Stauungspapille oder ähnliche Symptome.

Eine gefährliche Komplikation dieser Phase der Höhenanpassung ist das akute Lungenödem (Hurtado, 1956). Seine Pathogenese ist unklar. Die gründlichen Untersuchungen von Hultgren *et al.* (1961) konnten in keinem Fall eine Insuffizienz des linken Ventrikels nachweisen. Sicher bestehen Beziehungen zu den von Rotta *et. al.* (1956) durch Herzkatheteruntersuchungen nachgewiesenen Drucksteigerungen in der *Arteria pulmonalis* und zu der vermehrten Blutfülle der Thoraxorgane (Monge *et. al.*, 1955), eine Vermutung, die Kronecker schon 1903 äußerte. Hinzu kommen die Veränderungen der vegetativen Innervation, die in dieser Phase besonders intensiv sind.

Alle drei Formen der höhenbedingten Erkrankungen: Akute Höheninsuffizienz, Bergkrankheit einschließlich des Lungenödems und Monge'sche Krankheit lassen sich aus den normalen Phasen der Höhenanpassung ableiten. Die akute Höheninsuffizienz ist eine überschießende erste Phase, die Bergkrankheit eine Entgleisung der zweiten Phase, wahrscheinlich verbunden mit einer Störung des intermediären Stoffwechsels, die Monge'sche Krankheit zeigt alle Symptome der vollendeten Höhenakklimatisation in pathologischer Übersteigerung. In jedem Fall ist der Sauerstoffmangel als pathogenetischer Faktor beteiligt. Das klinische Bild wird aber weniger durch den augenblicklichen arteriellen Sauerstoffdruck als durch den augenblicklichen Zustand des Organismus und den Grad seiner Höhenanpassung bestimmt.

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THE ROLE OF ERYTHROPOIETIN IN THE POLYCYTHEMIA OF HIGH ALTITUDE

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Abstract – Three groups of experiments were carried out with the plasma and urine of natives of high altitude (4540 m) and sea level (Lima) in search for erythropoietin. The samples were tested in rats. (1) Erythropoietin was found in the serum of newcomers to high altitude 24 hr after arrival. (2) Evidence for an inhibitory factor was found in the plasma of altitude natives when brought to sea level. (3) The plasma of rabbits after exposure to 7400 m when given to rats caused a 3-fold increase in iron absorption from the intestines.

Zusammenfassung — Auf der Suche nach Erythropoetin in Urin und Plasma wurden 3 Gruppen-Experimente durchgeführt. Plasma und Urin stammten von Eingeborenen in 4540 m und auf Seehöhe. Die Prüfung der Proben erfolgte an Ratten. (1) Erythropoetin wurde im Plasma von Personen 24 Stunden nach Ankunft aus dem Tal in der Höhe gefunden. (2) Den Beweis für einen Erythropoese-Hemmungsfaktor ergab die Untersuchung des Plasmas von Bergbewohnern nach Ankunft in Lima. (3) Das Serum von Kaninchen, die kurze Zeit 7400 m Höhe ausgestzt waren, bewirkte bei Ratten einen 3-fachen Anstieg der Eisenabsorption aus dem Darm.

Résumé – On a examiné la présence d'érythropoétine parmi trois groupes de personnes: a) des indigènes vivant à 4450 m d'altitude, b) de nouveaux arrivés à cette altitude après 1, 3 et 8 jours, c) des habitants de Lima (au bord de la mer). Le plasma de ces individus fut fractionné et inoculé à des rats. Chaque bête reçut durant deux jours une dose correspondant à 4 ml de plasma. On injecta ensuite du ^{59}Fe i.p. et l'on examina au moyen d'échantillons de sang prélevés dans le coeur après 18 hr la part de Fe assimilée. La quantité de Fe assimilée était maximale pour les animaux qui avaient reçu du sang provenant de personnes arrivées depuis 24 hr en altitude (groupe b). Des extraits alcooliques d'urine provenant des mêmes personnes n'eurent aucun effet. Des rats exposés à l'altitude et des bêtes de contrôle reçurent du sang d'indigènes vivant à 4450 m d'altitude (groupe a) et arrivés au niveau de la mer depuis 1, 3, 10 et 20 jours. On a alors recherché la présence d'un facteur d'inhibition. On peut ainsi expliquer la diminution de l'érythropoèse. L'expérience précédente avait démontré qu'il existe un facteur humoral activant l'absorption du fer par l'intestin. On a également examiné au moyen de rats le sang de lapins exposés à l'altitude. La concentration en Fe^{59} était presque trois fois inférieure dans le sang de bêtes de contrôle que dans celui de rats ayant reçu du plasma de lapins ayant été exposés à l'altitude.

The polycythemia of high altitudes has been studied from many points of view but almost no attention has been given to the erythropoietie factor. Although it is generally accepted that in all cases of hypoxemia the erythropoietic factor is stimulated there are still some special problems in high altitude polycythemia. First, is there a detectable amount of erythropoietin in the circulating plasma and urine, both in acute and chronic exposure? Second, can the deglobulization that occurs, when high altitude polycythemic subjects are brought down to sea level, be explained solely on the basis of a decrease of erythropoietin or is there an inhibitory factor that produces a depression of red cell production? Third, does erythropoietin play a role in iron absorption during altitude changes?

(1) Regarding the problem of erythropoietin detection during high altitude exposure we have studied three groups of subjects: (a) natives of Morococha (4540 m); (b) newcomers to Morococha after 1, 3 and 8 days of exposure; (c) sea level subjects. The plasma obtained from each was processed by the method of Borsook (1954) and liophilized. The material was tested in rats. Each animal after two days of starvation received a dose equivalent to 4 ml of the original volume of plasma, for a period of two days. Twenty-four hours after the last injection, ^{59}Fe was given intraperitoneally, and 18 hr later blood samples from the heart were obtained. Red cell iron incorporation was studied.

Table 1. Plasma Erythropoietic Factor during Exposure to High Altitude

	Control at sea level	After 1 day	After 3 days	After 10 days	Natives of Altitude
Mean	5.5	9.0	5.5	5.4	4.2
±SE	0.38	1.3	1.4	1.2	1.2
Number or rats	8	7	5	8	7

Table 2. Erythropoietic Factor in Urine after High Altitude Exposure

	Control at sea level	After 1 day	After 3 days	After 10 days
Mean	5.4	5.1	4.9	6.4
± SE	0.8	1.2	1.3	1.4
Number of rats	7	7	5	6

The red cell iron incorporation was higher only in the group of rats that were injected with plasma filtrates of newcomers after 24-hr exposure to high altitude, compared to the control group receiving sea level plasma filtrate (Table 1).

Alcohol extracts of urine from the same groups of subjects was also tested in rats. Doses equivalent to 20 ml of urine were given daily in the same manner as in the plasma experiments. The results were negative in all the groups (Table 2).

These findings are similar to those found by Stohlman (1959) in rats exposed to simulated altitudes. They are also in agreement with the concept that erythropoietin is utilized by the erythropoietic tissue and that it increases in the circulating blood for a few hours only when there is a high production, or when it is not utilized, as in aplastic anemia.

(2) The possibility of the existence of an inhibitory factor to erythropoiesis (Krzymowsky and Krzymowsky, 1962) has been studied by testing in rats the plasma filtrates of high altitude natives brought down to sea level, after various periods of time: 1, 3, 10, and 20 days. The plasma filtrates were prepared by the method of Borsook (1954). The rats were previously stimulated by exposing them to a simulated altitude of 5500 m for 24 hr. After that, 1 ml of the material equivalent to 2 ml of the original volume of plasma was injected intraperitoneally. At the same time 1 μc of ^{59}Fe was given 4 hr later. Twenty-four hours after the injection of radioactive iron blood samples were obtained from the heart. As a control a group of rats which was exposed to 5500 m was given plasma filtrate from normal sea level.

The results showed that the mean value for the iron incorporation in red cells in the group of rats that were given plasma filtrate from polycythemic subjects was 35.3 per cent 1 day after arrival at sea level, 30.1 per cent in the 3-day group, 28.5 per cent in the 10-day group and 28.4 per cent in the 20-day group. In the group of rats receiving sea level plasma it was 41.0 per cent. The mean value differences between the sea level normal group and the 3-day, 10-day, and 20-day group was statistically significant (Table 3).

Table 3. Effect of Plasma Filtrate from Altitude Natives brought down to Sea Level in Rats Submitted to 5500 m

Group	Number of rats	Treatment	^{59}Fe uptake
I	13	sea level plasma	41.6 ± 2.76
II	7	24-hr plasma	35.3 ± 3.48
III	7	72-hr plasma	30.1 ± 4.04
IV	14	10-day plasma	28.5 ± 2.46
V	7	20-day plasma	28.4 ± 2.50

In a second experiment, 5 rats were injected with liophilized filtrate of plasma from high altitude natives 10 days after arrival at sea level. One millilitre of this material, equivalent to 4 ml of the original volume of plasma, was given for 7 days. At the end of the experiment a decrease of hemoglobin was observed in all the rats.

The difference between the mean values of hemoglobin before and after the experiment was 1.6 g per cent ($p < 0.05$) (Table 4).

Both experiments seem to indicate that an inhibitory humoral factor does exist in the plasma of high altitude natives brought down to sea level. The presence of such a factor would explain the depression of red cell formation that occurs in them.

Table 4. Effect of Plasma Filtrate from Altitude Natives after 10 days at Sea Level on Normal Rats

Number of rats	Days of treatment	Hemoglobin (g%) before treatment (Mean+SE)	Hemoglobin (g%) after treatment (Mean +SE)
5 ($p < 0.05$)	7	13.0 ±0.25	11.6 ±0.52

Table 5. Influence of Plasma Filtrate from Altitude and Sea Level Rabbits on Iron Absorption

	No. of rats	Percent ^{59}Fe appearing in blood (Mean +SE)
Plasma filtrate of altitude rabbits	11	19.9 ±2.6
Plasma filtrate of sea level rabbits	11	7.1 ±1.4

(3) It has been shown before that there is a close relationship between the level of red cell production and iron absorption during altitude changes, which suggests that the regulating mechanism of iron absorption must be closely related to that controlling erythropoiesis (Reynafarje, 1961). To test this hypothesis we studied rats that had received plasma filtrate from rabbits submitted to an altitude of 7400 m, using a control group of rats receiving sea level plasma filtrate (Table 5).

The rats that received plasma from high altitude rabbits showed an iron absorption three times greater than the group of rats given sea level plasma. However, it cannot be determined by this experiment whether the erythropoietin acts directly on the intestine to stimulate absorption or whether its role is simply to increase red cell production, which in turn might control iron absorption.

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THE EFFECTS OF AMBIENT AIR TEMPERATURE ON THE ACCLIMATIZATION OF RATS TO HIGH ALTITUDE

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Abstract – The mean body weight of male rats of different ages first decreased after ascent to high altitude (3450 m), then increased and continued to rise according to the growth pattern significant for different age groups. The length of the period of weight loss was shortest in 30-day-old rats (1 day) and longest in 7-month-old rats (34 days). There was a linear relationship if the period of weight loss was plotted against age on double logarithmic paper. The fall in mean body weight was enhanced when the rats were kept at a lower (10°C) or higher (28°C) ambient temperature instead of the normal room temperature. The weight loss period can be used as a parameter of the adaptability of the animals to high altitude.

Zusammenfassung – Das mittl. Gewicht von männlichen Ratten verschiedenen Alters zeigte einen vorübergehenden Verlust nach Übergang in die Höhe von 3450 m, ehe das ursprüngliche Gewicht wieder erreicht wurde und weiter anstieg, wie es den Altersklassen entsprach. Die Länge der Gewichtsverlustperiode betrug bei 30 Tage alten Tieren einen Tag, bei 7 Monate alten Tieren 35 Tage. Wenn die Werte auf doppelt logarithmischem Papier aufgetragen wurden, ergab sich eine lineare Beziehung zwischen Alter und Gewichtsverlustperiode. Der Abfall des mittl. Körpergewichts war verstärkt bei Ratten, die entweder bei 10° oder bei 28° C anstatt bei 22° C (übliche Raumtemperatur) gehalten wurden. Die Gewichtsverlustperiode kann als Parameter zur Bestimmung der Anpassungsfähigkeit der Tiere an die Höhe verwendet werden.

Résumé – Des rats mâles d'âges différents ont montré une perte passagère de leur poids moyen après avoir été transportés à une altitude de 3450 m. Ils ont ensuite repris leur poids initial puis ont augmenté de poids selon leur classe d'âge. La durée de cette perte de poids fut de 1 jour pour les individus âgés de 30 jours, de 35 jours pour ceux qui avaient 7 mois. Si l'on reporte les valeurs obtenues sur une trame doublement logarithmique, on constate une relation linéaire entre l'âge des rats et la longueur de la période de perte de poids. La baisse du poids moyen était en outre plus sensible pour les rats qui étaient soumis à des températures de 10° ou de 28° C au lieu de 22° C (température ordinaire d'une pièce chauffée). On peut utiliser la durée de la perte de poids comme paramètre indiquant les possibilités d'adaptation des animaux à l'altitude.

BELOW the critical environmental temperature of 27° C rats increase heat production linearly with decreasing temperature until the lower limit of temperature tolerance is reached (Weihe, 1964a, c). The increase in heat production is an adaptation process to the decrease of environmental temperature which lasts a certain time period before the new steady state is reached. This process can easily be investigated either directly by determining the heat production or indirectly by measuring the daily food consumption.

Rats taken to simulated or natural high altitudes reduce their food intake for a certain time (Altland, 1949; Timiras, Krum and Pace, 1957; Ulrich, 1962; Tribukait, 1963; Weihe, 1964b). The question arose as to whether this reduction of food intake could be influenced by changes of environmental temperature. Measurements of body weight and food consumption served in this study as parameters to determine the adaptability of animals to altitude and changes of temperature.

MATERIALS AND METHODS

Rats of the Wistar strain, kept for several generations in our breeding colony, were used. All animals were from the first litter of females mated at the age of 60 days. Weaning was at day 21 of lactation. In all experiments equal numbers of rats were caged in stainless steel basins, 43×32 cm and 20 cm high, with perforations on the front side and lid; wood shavings were provided as bedding. Water and food (Altromin R Standard diet) were given *ad libitum*. Food pellets were put in hoppers of which the daily food waste was less than 3 per cent. Room temperature 22° C, rel. humidity 35–70 per cent, artificial day from 7:00 to 19:00hr. Each animal was weighed daily between 8:00 and 9:00 hr. Food and water consumption per cage was measured. Individual and mean growth curves were computed so that rats of any age could be taken at any time from the colony in Bern (540 m) to be brought to the High Altitude Research Station Jungfraujoch (3450 m). All conditions in the animal quarters were alike at Jungfraujoch and Bern. Room temperature could be varied between 10° and 30° C. The experiments were carried out in the period from November 1962 to July 1963.

RESULTS

Figure 1 shows the 24-hr rhythm of the body weight in rats. The body weight is highest between midnight and 8:00 hr. There is a gradual decline of body weight in the resting phase during the day due to digestion, urination and defecation the lowest body weight being reached between 16:00 and 18:00 hr. With the beginning of the activity phase about 18:00 hr rats start eating and drinking again. Hence two body weights can be recorded:

(a) Body weight after feeding, i.e. 8:00 to 9:00 hr;

(b) body weight after resting, i.e. 16:00 to 18:00 hr,

of which (a) represents the amount of food and water consumed and the weight increment during the previous 24 hr, and (b) the weight increment only.

In these studies the morning weight was chosen because it best reflects the food and water consumption of the animal during the previous night.

After arrival at high altitude (3450 m) less food was consumed by the rats during the first and subsequent nights as shown in Fig. 2. The morning body weight — not the afternoon weight — was reduced due to a smaller food and water consumption during the previous night. In Fig. 2 the mean food consumption/rat/day is plotted below the mean weight curve. The period of reduced body weight in this group of

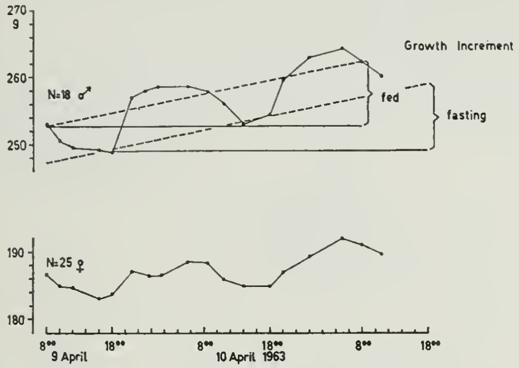

FIG. 1. 24-hr rhythm of body weight in male and female rats

rats lasted 9 days. After this period of reduced body weight the body weight curve increased slowly, but was certainly depressed in comparison with ground level controls during the entire 43-day stay at high altitude. Immediately after return to ground level the mean body weight curve increased steeply and so did the food

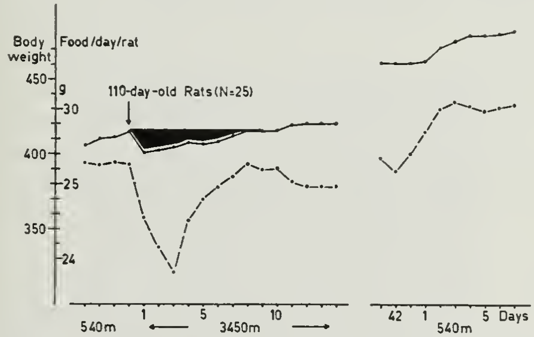

FIG. 2. Average loss of body weight and reduction of food intake in rats after arrival at high altitude and increase of body weight and food intake after return to ground level

consumption curve. The importance of this effect which results from reduced metabolic activity of the animals at high altitude will be described in detail elsewhere (Weihe, 1965d).

Groups of male rats of 5 different ages were taken to Jungfraujoch and the length of the period of reduced body weight was measured. The data are given in

Table 1. According to these data the length of the period of reduced body weight increased with age and body weight. There was no correlation between length of period of reduced body weight and body weight on the last day at ground level. However, when the length of the period was plotted against age on logarithmic paper a straight line was obtained (Fig. 3).

Table 1.

Age days	Weight g mean	Length of period of reduced body weight days mean $\pm$SE
32	90 ($N = 22$)	1
66	315 ($N = 24$)	4.1 $\pm$0.42
108	415 ($N = 25$)	9 $\pm$1.3
160.	470 ($N = 22$)	24 $\pm$1.7
216	520 ($N = 13$)	35 $\pm$2.8

The results shown in Table 1 and Fig. 3 formed the base line for the adaptation pattern of male rats of different ages to high altitude which could be used to study the effects of changes of temperature under otherwise similar conditions.

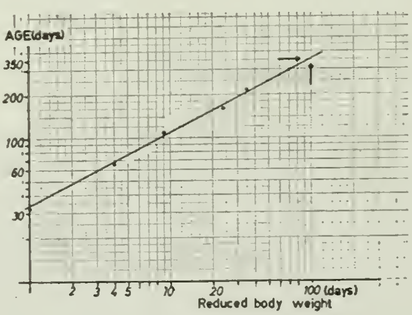

Fig. 3. Relationship between period of reduced body weight and age on logarithmic paper

Male rats, aged 120 days, were kept at three different temperatures, 28°. 22°, and 15° C, after arrival at high altitude. The previous maintenance temperature at ground level was 22° C. In Fig. 4 the mean food consumption/rat/day at different times after arrival is plotted. It was found that the reduction of food intake of the animals at 28° C remained unchanged during the first 16 days. Taking these lowest food consumption rate data 8 (mean of day, 7, 8, and 9) and 16 days (mean of day 15, 16 and 17) after arrival at high altitude as the base line it was found that at 22° C the food consumption increased gradually during this time period. The same was seen at 15° C to which temperature the animals had never been exposed before. The increase in food consumption was faster and more pronounced. The slope of the line given by the mean food consumption at the three temperatures 16 days after arrival at high altitude remained unchanged during

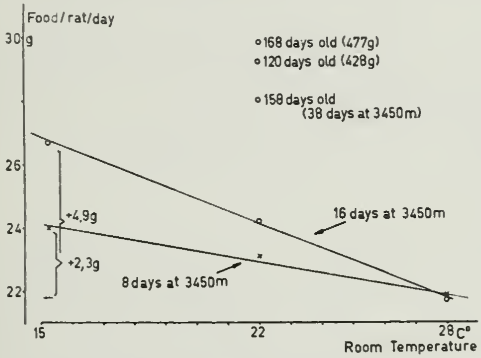

FIG. 4. Adaptability to high altitude at different room temperatures

the entire 40-day stay at altitude. However, there was a gradual parallel upward movement of the line towards the values for mean food consumption at 22° C as indicated. At the end of the 40-day stay at altitude it was still more than 2 g food /rat/day below the line of the mean of the original ground level values and the values 8 days after return to ground level. According to this finding the length of the period of reduced body weight should have been alike for the rats at the three different temperatures. This was not so. The period was shortest at 22° C with a mean of 10 days, longest at 15° C with a mean of 18 days and had a mean of 14 days at 28° C.

In an additional experiment 37-day-old rats were kept at temperatures from 12° to 30° C. Optimal food consumption at high altitude as compared with ground level controls was reached within 8 days and growth rate was not depressed at any time besides the reduced body weight for one day after the first night at altitude. Hence young rats acclimatize very well to altitude and temperature changes in contrast to older rats.

DISCUSSION

The determination of the length of the period of reduced body weight of rats at high altitude was used here as a method for studying the effect of temperature on adaptation to high altitude. The method is based on the well known fact that the body weight of animals after exposure to high altitude is below the previous values. The length of the acclimatization period to high altitude, as based on this parameter, depends on the age of the animals (Fig. 5). The length of the period of acclimatization to changes of temperature also depends on the age of the animals, being short in young and long in old animals (Weihe, 1965c). It was found that in animals which were exposed to the altitude of 3450 m and changes of temperature simultaneously both adaptation processes took place. In young rats both adaptation processes took place rapidly and the growth curve was unchanged.

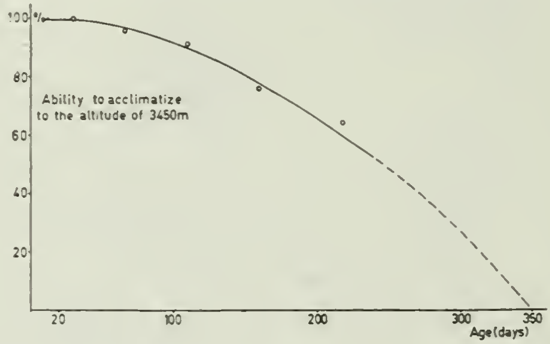

Fig. 5. Ability of rats to acclimatize to high altitude in per cent based on period of reduced body weight

In older animals, however, for which the length of the period of reduced body weight as a parameter of high altitude acclimatization is longer than a week, changes of environmental temperature above or below the maintenance temperature were reflected in a prolongation of the length of the period of reduced body weight and food consumption. Cold did not act as a stimulant to food intake nor did heat, in which less food is required, obviate the reduction of food intake. In older rats the additionally induced adaptation to change of temperature has an impeding effect on the acclimatization to high altitude as the length of the period of reduced body weight is prolonged. According to the curve of adaptability of rats of different ages to the altitude of 3450 m in Fig. 5 change of temperature may lead to a steeper decline of the curve. More data, using rats older than 120 days, are needed to establish the curve on paired factor acclimatization.

The findings are in agreement with the previous findings on cross acclimatization (Fregly, 1954; Hale and Mefferd, 1958). This cross acclimatization does not apply to young rats in the first few weeks after weaning with their high adaptability.

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SOLAR RADIATION AT HIGH ALTITUDE

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In a review of data on heat load (cal/cm^{2}min) at different altitudes up to 5000 m, direct solar radiation (I), scattered sky radiation (D) and global radiation (G) were discussed. I increases with solar altitude (γ) and altitude above sea level (h). $I\gamma$ is more intense before than after noon due to the purity of the atmosphere. The heat load for 2 elevations is clearly higher for the altitude of 4900 m than for 2900 m during the months June to September, while it is almost the same at both altitudes during the remaining months. Like I, the total energy of D also depends on γ and h. On clear days $D\gamma$ is small. Atmospheric conditions have not been studied sufficiently, hence little material is available on $D\gamma$. It is anticipated that the amount of D decreases with h. Available data are significantly dependent on the local atmospheric conditions and show no regularity. D was low in summer at one observation place because there was clear weather during this period. Extreme values of D can be measured which are as high as those of I at the same place. This of importance in human physiology because I is direct irradiation while D irradiates the body from all sides. D increases with increasing cloudiness. G is affected by the same factors as I and D. Energies higher than the solar constant are measured in cases where clouds reflect a part of the radiation in the direction of the measuring instruments. These observations apply to all parts of the solar spectrum.

SUMMARY REPORT

W. H. WEIHE

Of the ten papers submitted to this working group two could unfortunately not be presented by the authors themselves (T. R. A. Davis and C. Reynafarje).

The working group on Natural and Acquired Acclimatization at High Altitude met for one full day during the congress. The number of participants was much larger in the morning than in the afternoon because fewer sessions of working groups on related topics were held in the morning. Nevertheless, there were very lively discussions after each paper.

The variety of topics was wide. They ranged from solar radiation in the view of the physicist (Robinson) to such specific high altitude effects as those on erythropoiesis (Reynafarje), cerebral vascular circulation (Betz and Wünnemann) and oxygen transport (Blatteis), specific adaptation patterns (Davis *et al.*; Clegg and Harrison; Weihe), and pathological phenomena (Grover, Vogel and Blount; Alexander and Will; Jungmann).

The new approach in high altitude biometeorology was seen during the meeting in the emphasis on multifactorial investigations taking into account the various meteorological factors of the high altitude climate. This was expertly introduced in the review on solar radiation by Robinson, who described the enormous heat load on the radiated part of the body at high altitudes and steep temperature gradient between the radiated and the non-radiated part with direct solar radiation and the change in this with scattered radiation. Nothing could be contributed to the physicist's statements by the physiologists of the group as very little work on the physiological effects of solar radiation has been done recently.

New information was presented about adaptation to temperature changes at high altitudes. Of particular importance was the investigation of cold acclimatization in low and high altitude acclimatized Indians and Tibetans by Davis *et al.* which can serve as a model for future studies. Their results showed the impairment of certain mechanisms of cold acclimatization at high altitude, regardless of heat production and thermal balance. Less specific but leading in the same direction were the experiments by Weihe with rats in which the importance of the age of the individual as a factor in adaptability was stressed.

Though every study is based on specific parameters one is tempted to derive a profound generalization from it. Clegg and Harrison used the term "fitness" in their experiments on the weight of mice exposed to three simulated high altitudes in decompression chambers. Though there was agreement in the group discussion on this and the following paper by Weihe that the term fitness can be heuristic and of some practical value there was unanimous opposition to its general usage. Fitness may refer to many physiological functions with widely varying time courses of adaptation and of different importance for survival and maximal efficiency. Therefore, whenever fitness is mentioned it should be stated to which parameter it refers.

From all the contributions to the working group it was apparent that long-term exposures of animals and man, possibly under natural conditions, is attracting increasing attention. Of particular interest in this respect are the investigations of the group of the University of Colorado Medical Center on the population of the city of Leadville, Colorado, at 3100 m. The population of this city can be used for the study of the development of natural acclimatization at high altitude as the parents of all the families came from low altitude. The studies on pulmonary hypertension presented by Blount dealt with only one parameter of many that could be considered. Similar studies can easily be carried out with cattle residing and native to high altitude as used by Blatteis in his investigations on oxygen transport during the first 30 days after birth and referred to by Alexander in his studies with Will on brisket disease.

Dr. Alexander stressed the increased pulmonary vascular resistance and the progressive hypertrophic changes of the muscle in the media of the small pulmonary arteries and arterioles in cattle with high altitude induced pulmonary hypertension. This finding of an increase in the medial muscular mass of the lungs may also lead to a better understanding of chronic mountain sickness in man. The classification of the vaguely defined complex "mountain disease" into three distinct types of mountain sickness based on symptoms and signs as reported in the literature was put forward by Jungmann. This classification may pave the way for more specifically directed studies on man and will serve as a hypothesis in the search for similar phenomena in laboratory and domesticated animals.

The wide scope of the topics left everyone with the impression that high altitude physiology is progressing on many fronts and has begun to consider other factors of the physical environment besides reduced partial pressure of oxygen. Methods were not a topic of discussion in the working group. Hardly any physiological or pathological function of the body – besides erythropoiesis and perhaps respiration which was not dealt with by this working group – has been so thoroughly investigated that programs for comparative investigations in different climatic zones and different races using standard methods and conditions can be carried out.

Great progress can be expected when the various factors significant for high altitude climate (low temperature and humidity, strong solar radiation and winds) are more fully investigated in future studies. For this reason the participants of the working group agreed unanimously to meet again during future congresses of the International Society of Biometeorology.

BASIC MECHANISMS OF PHYSIOLOGICAL ADAPTATION TO THE METEOROLOGICAL ENVIRONMENT

Chairman: H. Hensel

GENERAL ASPECTS OF PHYSIOLOGICAL ADAPTATION

H. HENSEL

Physiologisches Institut, Universität Marburg,
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It is a great pleasure for me to welcome you to our Working Group on "Basic Mechanisms of Physiological Adaptation to the Meteorological Environment". Research in this field has hardly left the era of mere description, and our present concepts of adaptive processes are largely based on indirect evidence and speculation.

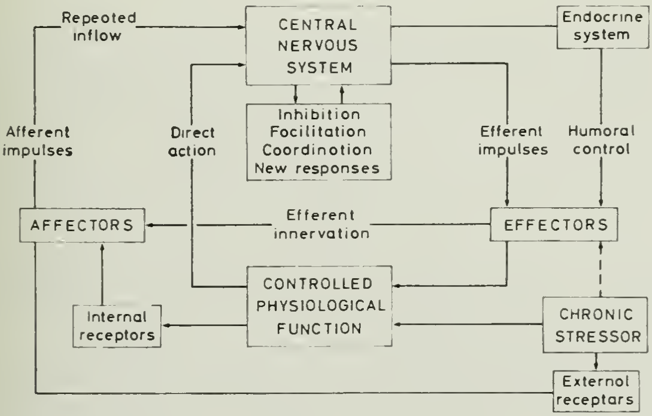

Fig. 1.

To begin with, it seems useful to consider some general aspects of adaptation and to define the terminology used in this field. Physiological adaptation is part of the fundamental ability of organisms to maintain homeostasis or stability. Adaptative processes can be characterized as temporal biological events following a deviation of an environmental factor, be it periodic or aperiodic.

Let us consider the case where an environmental factor, such as temperature, is shifted rectangularly with time to a new constant level (Fig. 1). After a transient deviation, certain physiological values or functions tend to normalize, i.e. to move again towards the initial level. The time course of this normalization can vary considerably with the biological system involved. From this it follows that an adapting physiological function can be kept at a constant level when the stimulus increases as a function of time. The method of assessing adaptation by changing the environmental condition E continuously with a certain slope dE/dt has the advantage of preventing shock reactions, damage, or death of the organism before adaptations have developed.

Stabilization or normalization of a physiological function in a changed environment is only possible when other functions – called adaptates – deviate from their initial value as long as the external stimulus or stressor is being maintained. The time course of normalization depends on the temporal development of adaptates. For instance, during a constant heat stress, the core temperature in man rises initially but then normalizes within the next few days when adaptates, such as more effective sweating, are developing.

Usually the term adaptation is restricted to modifications that enhance survival or seem "favorable" to the organism. However, the meaning of this definition is not clear, and in many cases it is impossible to decide whether an adaptive change is favorable or not, this decision being largely a matter of teleological speculation.

When nerve accommodation and adaptation of sensory receptors are excluded, physiological adaptations can be classified by their time course as follows.

(1) Acute regulations against external disturbances occurring within time intervals ranging from seconds to minutes, sometimes hours.

(2) Slower adaptive responses of organisms to changes in the environment ranging from hours to months, sometimes even years. These responses are restricted to the single individual and included in the terms acclimation, acclimatization, and habituation.

(3) Adaptation in the evolutionary sense – nongenetic transmission and selection of genetically adapted types – is the slowest process, involving many generations and time amounting perhaps to millions of years.

The topic of our working group will be mainly restricted to the second group of adaptations: acclimation and habituation. Adaptations are not always single events reaching a new steady state aperiodically after the environment has changed. They may involve a sequence of adaptive responses with various time constants, the early processes often being overshooting and transient reactions. When the exposure is prolonged, the initial adaptates may normalize, while more stable and specific adaptive responses will appear. An example is the sequence of adaptates in homeotherms during prolonged cold exposure: (a) shivering, (b) nonshivering thermogenesis with transitory changes in the endocrine system, (c) perhaps nonshivering thermogenesis with the normal endocrine system, (d) trophic changes in the integument which may occur simultaneously with *c*.

Biological homeostasis or stability, whether cellular or integrated, autonomic or behavioral, is maintained by feedback controls that respond to deviations from a physiological state. The nervous system is an essential part of homeostatic regulations in higher organisms. Adaptations can be considered as modifications of homeostatic regulations that are already present in the acute responses, but very little is known about the nature of these modifications and the nervous processes involved in slow adaptation.

There are various theoretical possibilities, by which a nervous control mechanism can be changed under the influence of a chronic stressor (Fig. 2). We have good reasons to assume that the decisive events take place in the central nervous system rather than in the periphery. In some cases, especially in *poikilo-organisms*

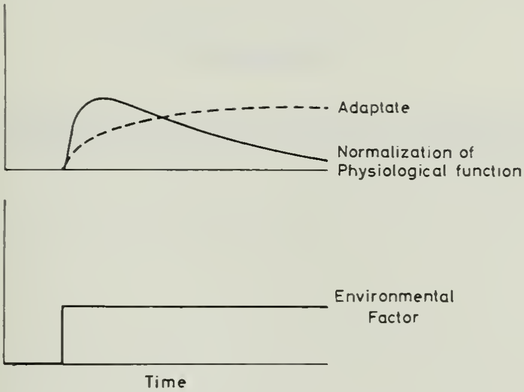

FIG. 2.

the stressor can reach the central nervous system directly; but even then the adaptive changes might be due to afferents from receptors. In *homeo-organisms*, where temperature, osmotic pressure, and other characteristics inside the body differ considerably from those of the surroundings, the effect of the stressor may reach the central nervous system directly or by a prolonged or repeated inflow from receptors. In the second case, adaptation is closely related to learning, conditioning and habituation. It is a change in response of the organism depending on previous information or experience.

Various mechanisms might be involved in these changes. The afferent flow of nervous information can be influenced at various levels of the central nervous system by efferent impulses originating in the brain. Second, higher centers can change the sensitivity of peripheral receptors by efferent innervation. A third possibility is the change in synaptic transmission itself. Disuse of a synaptic pathway leads to inhibition, whereas repetitive stimulation causes facilitation of transmission. Besides inhibition and facilitation, more complex events seem to occur in the central nervous system in the course of acclimation, such as changes in the response pattern, shift in the level of regulation, and improved coordination of somatic and vegetative functions.

There is no satisfactory electro-physiological evidence as to the question of local acclimation of receptors. Many receptors are probably firing throughout the life-time of an organism, even when the external conditions are kept constant. Such steady discharges are well established in thermoreceptors. Thus we can at least exclude a local receptor acclimation in the sense of a complete cessation of impulses. If we take for granted that information from receptors can induce acclimation, then a complete receptor acclimation would be unlikely from a theoretical point of view. In order to maintain adaptation, it is necessary to maintain afferent signals as long as the stressor is present. In habituation, where repeated stimulation during several days leads to a gradual diminishing response, local adaptation of receptors has been excluded.

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SIMILARITIES AND DIFFERENCES DURING CHRONIC EXPOSURE TO DIFFERENT STRESSORS

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Abstract – Cats with chronically implanted heat conductivity probes for recording local cerebral blood flow were exposed for some weeks to the following stressors: (a) 8 or 10 per cent O_2, (b) 3 or 5 per cent CO_2, (c) noise. At the beginning of the exposure cerebral blood flow increased, later it decreased again and often reached its initial level. The decrease during the course of adaptation was not constant. The slope showed periodic deviations from the mean values. The reaction to the various stressors differed in dura tion and in the extent of the increase which depended on the intensity of the stressor.

Zusammenfassung – Katzen, bei denen die Gehirndurchblutung mit Wärmeleitsonden fortlaufend registriert wurde, wurden über mehrere Wochen belastet mit: (a) 8 oder 10% O_2, (b) 3 oder 5% CO_2 und (c) Lärm. Während der Belastungen traten Änderungen der Gehirndurchblutung auf. Die Gehirndurchblutung stieg initial an und sank im Verlauf der Gewöhnung wieder ab. Der Abfall der Durchblutungskurve war nicht in allen Fällen gleichmässig; in manchen Fällen traten periodisch wiederkehrende kurzfristige Anstiege auf. Unterschiede bestanden in der Dauer des Abfalls der erhöhten Durchblutung und in der Zeitdauer der periodischen Durchblutungsänderungen. Die Dauer des Abfalls war von der Intensität des Stressors und von unterschiedlichen Ausgangsbedingungen abhängig.

Résumé – Des chats auxquels on a enregistré de façon continue la vascularisation sanguine du cerveau au moyen de sondes thermiques furent exposés à différents milieux défavorables durant plusieurs semaines. Il s'agissait: (a) d'un excès de CO_2, (b) d'un manque d'oxygène et (c) d'un bruitage violent. Dans ces trois cas, on a constaté des modifications de la vascularisation du cerveau au cours de la période d'adaptation. La dite vascularisation a tout d'abord augmenté pour diminuer à nouveau ensuite. Cette baisse de la courbe de vascularisation ne fut cependant pas régulière. On y a constaté au contraire de brèves périodes de recrudescence se répétant plusieurs fois. Les différences individuelles et relatives au milieu se sont surtout manifestées dans la durée nécessaire au retour à une situation normale et dans l'intervalle des variations périodiques de recrudescence de la vascularisation. La durée du retour à une situation normale est fonction de l'intensité du facteur nuisible et de différences constatées dans l'état initial des individus.

DURING adaptation the reactions to repeated stimulations are modified. Because of the great number of normal and pathological chronic stimulations during life the "adaptates" are very different. Nevertheless some reactions are similar during exposure to different stressors. On the other hand chronic exposure to two stressors can cause cross-reactions. It is known that in chronic hypoxia with CO_2 excess the respiratory volume and the frequency of respiration increase, whereas the plasma bicarbonate decreases in hypoxia alone (Luft, 1941; Opitz, 1941) but increases with CO_2 excess (Schaefer (1949, 1958).

Acute exposure to CO_2 excess and acute O_2 deficiency led to increases of cerebral blood flow and was seen by Kety (1948), Schmidt (1950), Schneider (1953), Noell and Schneider (1942, 1943). Acute exposure to noise also produced increases of cerebral blood flow (Betz, 1963).

Some experiments on the modification of cerebral blood flow (CBF) of cats during chronic exposure to various stressors are reported here.

MATERIALS AND METHODS

Recording local cerebral blood flow by means of permanently implanted heat conductivity probes made it possible to measure CBF during adaptation.

The probes remained within the brain of the cats for more than a year without restricting their freedom of movement. Therefore, the reactions of local CBF during chronic hypoxia, chronic CO_2 excess and during chronic noise, which upset the animals emotionally, could be recorded continuously.

The heat conductivity probes were implanted 4 to 6 weeks before the beginning of the experiments. Blood flow was measured within about 0.2 ml of brain-tissue. We recorded local blood flow mainly within the thalamus or hypothalamus and on the cortex (for details see Betz and Hensel 1962). Thirty cats were used. At the beginning of the experiments the cats were first acclimatized for a few days to their new environment. They were kept in partially glazed boxes in which they could move freely.

Hypoxia was produced by blowing nitrogen into the boxes and CO_2-excess by blowing CO_2 into the boxes. The cats received the mixtures with low O_2 (8 or 10 per cent) and high CO_2 (3 to 5 per cent) for at least 4 hrs daily. The noise was produced by hammering rythmically on a box made of thin metal.

RESULTS

Chronic CO_2 Excess

Figure 1 demonstrates the course of local cerebral blood flow in a single experiment in which the cat was exposed to 3 per cent CO_2 daily for 4 hr. Initially, there was a sudden marked increase in cerebral blood flow as in acute exposure experiments. During the daily repeated exposures the extent of the increase gradually diminished.

The mean values of the experiments on 3 cats, which received 5 per cent CO_2 daily for 4 hr are represented in Fig. 2. The initially high CBF decreased in the course of some days.

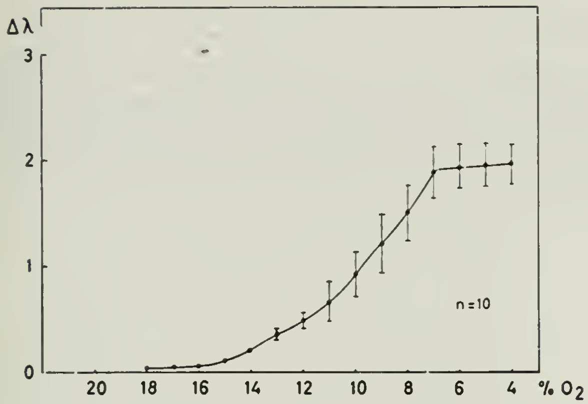

Fig. 1. – Effect of breathing 3 per cent CO_2 for 4 hr daily on the cerebral blood flow of a cat. On day 1, 5 and 11 of exposure

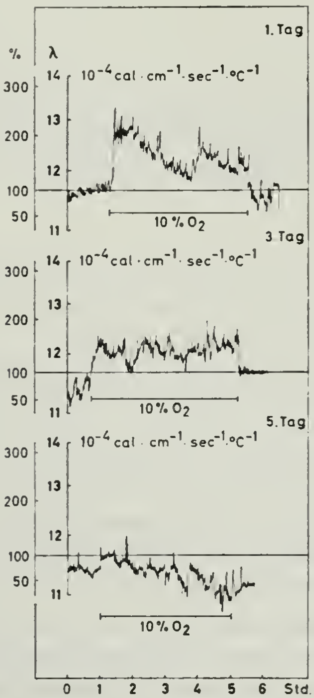

Fig. 2. – Mean values of cerebral blood flow during exposure to 5 per cent CO_2 for 4 hr daily in three cats. The x-axis represents the initial value

Chronic Hypoxia

The CBF increased in acute hypoxia and decreased again slowly in chronic exposure experiments. Figure 3 shows the average changes of CBF during exposure to 10 per cent O_2 and to 8 per cent O_2 for over 4 hr daily. In both groups of 10 cats each reactive periodic changes of the CBF could be seen.

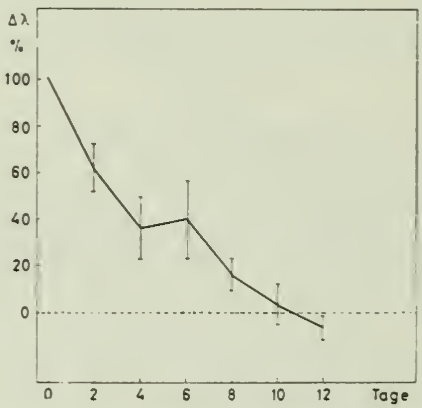

Fig. 3. – Mean course of local cerebral blood flow within the thalamus during adaptation to 10 per cent O_2 (10 cats) and 8 per cent O_2 (10 cats). Exposure time: daily 4 hr

Noise

With repeated periods of noise, lasting 1 min each, the increase of CBF during each noise period diminished in the course of time. Figure 4 demonstrates that no increase of CBF could be recorded after 70 min.

If the noise was produced continuously without interruption, the CBF returned faster to its initial value. Figure 5 represents the result of a 28-day experiment. Each day noise was produced until the initially increased blood flow had returned to control values. These noise periods were repeated 5 times daily with an interval of 10 min between the noise periods. In the experiment, represented by Fig. 6, there was only a small increase in CBF, after 28 days on this schedule, and the flow returned to normal within a few minutes. There were marked differences between individuals in these experiments.

In the three types of experiments the following similarities were seen:

(1) At the beginning of the action of the stressor, CBF increased. The extent of the increase depended on the intensity of the stimulation. Intensifying the stimulation led to an increase of the reaction until a maximum was reached. Further increase of the hypoxia and CO_2 excess led to an abrupt decrease of CBF under the signs of circulatory collapse.

Chronic exposure to one of the stressors caused a decrease of the initially increased CBF in all cases.

(2) The trend of the CBF curve was not constant. In all the experiments there were periodic changes after the first high increase. The increased reactions usually occurred again between the 3rd and 6th day of the experiment. At this time the reaction of the CBF to CO_2 deficiency and CO_2 excess was already diminished. In the noise experiment, these periods had another frequency.

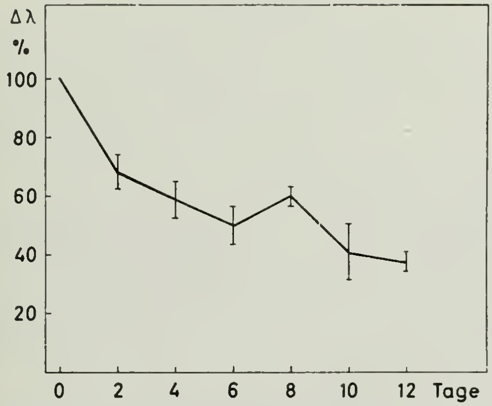

Fig. 4. – Increase of cerebral blood flow during noise. The single columns represent the increase of cerebral blood flow during a noise period of one minute. Interval between the single noise-series: 1 min

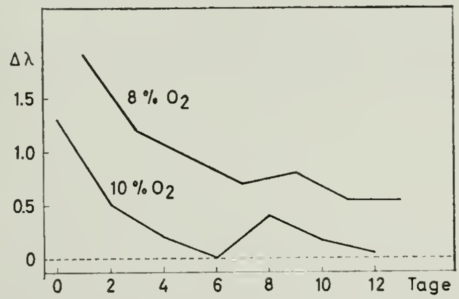

Fig. 5. – Increase of cerebral blood flow and time for return to initial value during noise series. Comparison of the reactions on the first and 28th day of the experiment. Interval between the noise-series: 10 min

(3) In preliminary experiments we saw similar reactions of pulse rate.

The following differences were recorded:

(1) The duration of the increased CBF depended on the intensity of the stressor and varied for individuals. In some experiments continuous noise led to an increase lasting one hour but in other cats the same kind of noise produced only a short and small increase during the first noise-period.

(2) The duration of the increased CBF also differed with the various stressors; 8 per cent O_2 caused a longer lasting increase than 5 per cent CO_2, and this again caused a longer lasting increase than 10 per cent O_2 or 3 per cent CO_2. All these stressors were more effective than noise. This is the usual result; however, there may be deviations.

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THE MECHANISM OF COLD-INDUCED HEAT PRODUCTION IN NEWBORN MAMMALS

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Abstract – Electromyographic and metabolic studies in unanesthetized newborn guinea pigs showed that during the very first days of life, electrical activity of the musculature remained practically at zero level when the animals were exposed to a cold environment of 8° and 16° C. Oxygen consumption rose to 200 to 300 per cent over basal rate. From the second week of life onwards rhythmic discharges from the musculature could be recorded under the same temperature conditions. The cold-induced elevation of oxygen consumption could be markedly reduced in young newborn guinea pigs by *hexamethonium-bromide* (an agent known to block non-shivering thermogenesis), whereas later on, when shivering was present, the effect of that drug was much less. Similar results have been obtained in kittens. According to these results, temperature regulation of young newborn mammals resembles that of *cold-adapted adult* subjects. It is suggested that the development of non-shivering heat production in the course of cold-adaptation might be thought of as a re-manifestation of the normal neonatal heat production mechanism.

Zusammenfassung – Electromyographie und Stoffwechseluntersuchungen bei nicht narkotisierten neugeborenen Meerschweinchen zeigten innerhalb der ersten Lebenstage während Kältebelastung bei 8° und 16° C keine Steigerung der elektrischen Muskelaktivität, obgleich der O_2-Verbrauch unter diesen Bedingungen um 200 – 300 Prozent höher als der minimale O_2-Verbrauch war. Erst von der 2. Lebenswoche an Traten unter gleichen Umgebungsbedingungen Salven von Aktionspotentialen in rhythmischer Folge auf. Ferner konnte der durch Kälteeinwirkung gesteigerte O_2-Verbrauch bei jungen Meerschweinchen durch Hexamethonium-Bromid (Blocker der chemische Thermogenese) reduziert werden, während bei älteren Tieren, bei denen Muskelzittern schon ausgebildet war, nur eine geringe Reduktion zu erzielen war. Gleiche Befunde wurden auch an jungen Katzen erhoben. Nach diesen Untersuchungen ist das thermoregulatorische Verhalten neugeborener Säugetiere wie das von *kälteadaptierten ausgewachsenen* Tiere. Man konnte demnach die Ausbildung der chemischen Thermogenese im Verlauf der Kälteadaptation als Wiederbelebung eines in der Neugeborenenperiode vorübergehend manifesten Mechanismus auffassen.

Résumé – Des recherches basées sur des électro-cardiogrammes et l'évolution du métabolisme de cobayes nouveaux-nés non endormis n'ont démontré, au cours des premiers jours de la vie, aucune augmentation de l'activité musculaire électrique dans une atmosphère refroidie entre 8° et 16° C, bien que la consommation en oxygène ait augmenté de 200 à 300 pour cent par rapport au minimum. Dès la deuxième semaine d'existance, on a pu enregistrer des détentes rythmiques de la musculature dans des conditions thermiques identiques. La hausse de consommation en oxygène due au froid peut être nettement réduite chez les cobayes nouveaux-nés par absorption de bromure d'hexaméthon (agent connu pour ses effets de blocage de la thermogénèse chimique). Chez les bêtes plus âgées, c'est à dire celles qui présentaient déjà des frissons, on n'a pu provoqué qu'une réduction insignifiante de la consommation en oxygène par ce moyen. On a en outre obtenu des résultats semblables sur de jeunes chats. D'après ces recherches, le comportement de la thermorégulation des mammifères nouveaux-nés est semblable à celui de bêtes plus âgées mais adaptées au froid. On pourrait ainsi admettre que le développement de la thermogénèse chimique constatée au cours de l'adaptation au froid n'est que la réapparition d'un mécanisme physiologique qui se manifeste passagèrement et naturellement durant une courte période suivant immédiatement la naissance des individus.

Under long-term cold exposure shivering is replaced by the more economical chemical thermogenesis ("non-shivering heat production") as has been demonstrated by studies in rats (Hart, Heroux and Depocas, 1956; Hsieh, Carlson and Gray, 1957) and in man (Davis, 1961). These studies confirm an old concept according to which shivering is thought of as the "more primitive" mechanism of heat production in comparison with chemical thermogenesis, which seems to presuppose some "practice" of cold defense reactions (Giaja, quoted by Thauer, 1958). It might, therefore, be presumed that temperature regulation at the time of birth is characterized by a preponderance of shivering, since the neonata has never experienced cold environmental conditions. It has been known for a long time, however, that newborn mammals as well as the human newborn infant (Mordhorst 1933; Brück 1961) do not display visible shivering at the time of birth and yet are able to increase heat production considerably when they are exposed to a cool environment. Consequently, either chemical thermogenesis or increased muscle tone without visible shivering must account for the increased oxygen consumption caused by cooling. Electromyographic and metabolic studies were undertaken in newborn guinea pigs and kittens in order to obtain conclusive information about the particular mechanism of cold-induced heat production in newborn mammals. (cf. Brück, 1963).

MATERIALS AND METHODS

Unanesthetized guinea pigs were repeatedly examined during the age period from 0 to 54 days. In some cases the first examination was carried out within the first hours of life. For the sake of comparison, 4 kittens of various ages were studied in addition. Birth weight of the guinea pigs ranged between 80 and 110 g. The oldest animals had reached a weight of 300–400 g when they were examined.

For the determination of metabolic rate an open system was used. The animals were placed in a climatized Plexi-glass chamber; fresh air was sucked through the chamber and led to a gas-analyzer* (Fig. 1). O_2-consumption, CO_2-production, colon temperature (at a depth of 5 cm from anus), and chamber temperature were continuously recorded. In principle the set-up was similar to that previously used for studies of newborn infants (Brück, 1961; Brück and Hensel, 1958).

* Hartmann & Braun AG., Frankfurt/Main, Germany.

For the determination of the electrical activity of the musculature needles of stainless steel were inserted into the thigh muscles. The electric signals were amplified and recorded by a Tönnies-EMG-Integrator.*

The electrical activity was continuously observed and recorded for one min every 10 min. By planimetry of the curves, representing the product of frequency of amplitudes (cf. Fig. 2), the mean electrical activity was obtained for every 1-min period.

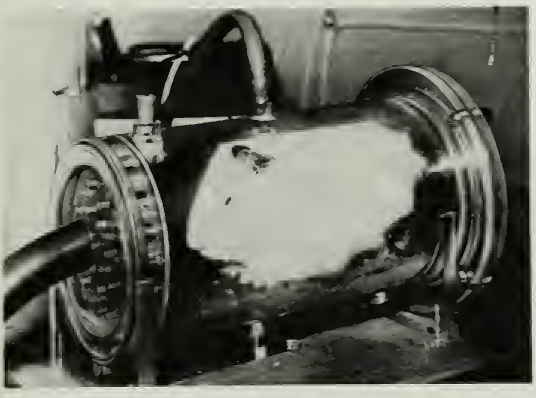

FIG. 1. Climatic respiratory chamber. The tube is double-walled; water circulates through it and is kept at a desired temperature by means of a thermostat

The cold exposure tests used for guinea pigs consisted of 1 hr at 16° C, and 8° C, respectively; in addition, minimal metabolic rate was determined at thermoneutral temperature (32° C). The kittens were exposed to 26° or 18° C. Minimal oxygen consumption of the kittens was determined at 32 to 34° C, depending on age.

In one group of guinea pigs and in all the kittens the effect of hexamethonium-bromide was studied. The drug was dissolved in 0.9 per cent saline and injected subcutaneously at a dose rate of 10 mg/kg; in a few cases the dose rate was increased up to 35 mg/kg.

RESULTS

Relationship of Oxygen Consumption and Electrical Activity in Guinea Pigs

During the first few days of life electrical activity, as a rule, has been found to be very low at all test temperatures (Fig. 2). There were periods lasting several minutes during which hardly any single action-potential could be detected, whereas from the second week onwards rhythmic discharges occurred during the cooling periods (Fig. 2). Since the animals were not being restrained they could move freely and did so occasionally. Electric discharges were produced by active movements in

* Dr. Tönnies, Freiburg/Br., Germany.

young animals too. However, since the animals were keeping quiet for long periods, active movements could not have accounted for the high oxygen consumption that was sustained over the whole cooling period. This may be seen from Fig. 3: on the

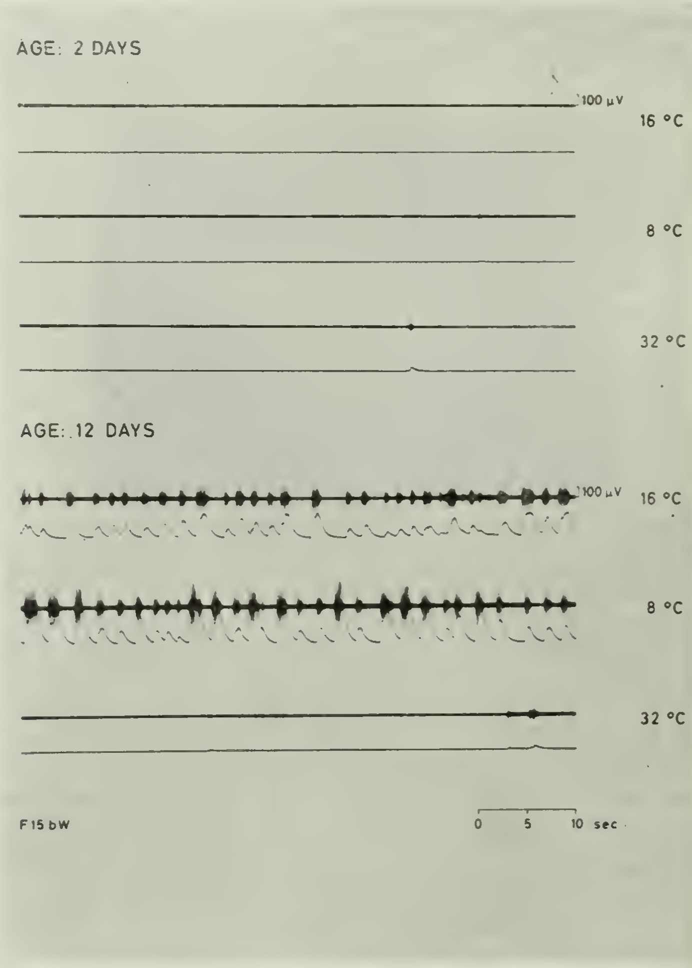

Fig. 2. Electromyograms from a guinea pig examined on the 2nd and 12th day of life at 3 different environmental temperatures (as indicated on the right side). The lower curves on each record represent the integrated EMG (mV c.p.s)

second day of life, oxygen consumption was increased by about 200 per cent during the whole cooling period, although the electrical activity remained at zero level in 10 out of 12 reading periods; on the average, electrical activity was no higher during

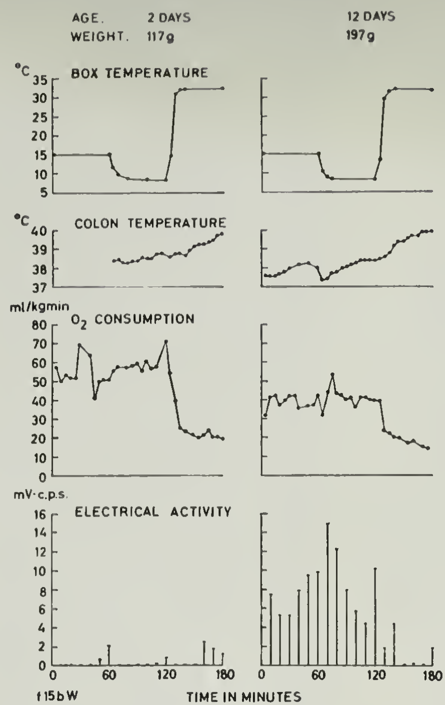

FIG. 3. The effect of different environmental temperatures on oxygen consumption and electrical activity of a guinea pig at day 2 and day 12 of life (same subject as in Fig. 2)

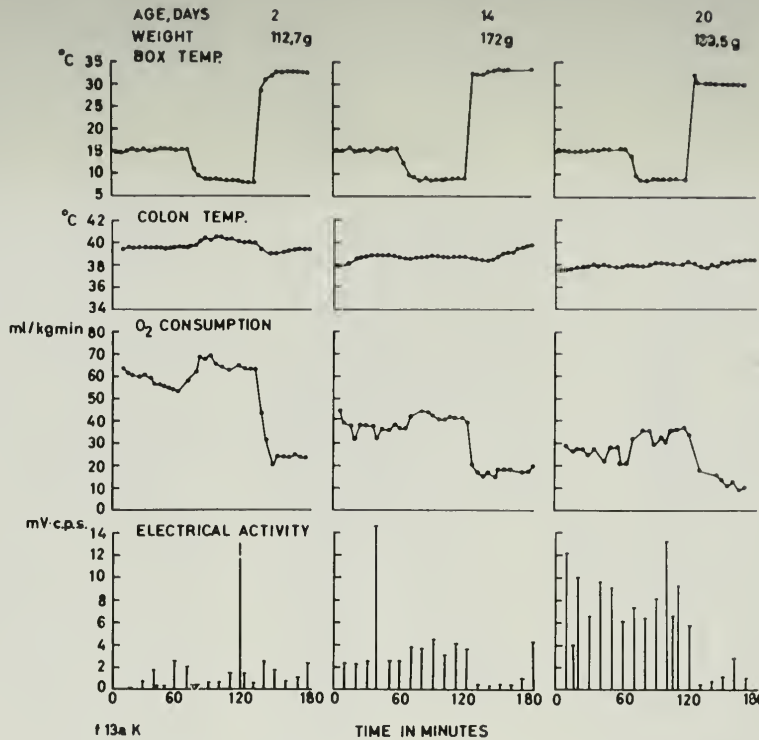

FIG. 4. The gradual increase of the shivering response during the first weeks of life in a guinea pig. The exceptionally high electrical activity at two recording periods were caused by active movement

the cooling period than at thermoneutral temperature. In contrast, on the 12th day of life (Fig. 3) electrical activity was elevated during the whole cooling period and was accompanied by visible shivering. The occurrence of shivering, however, did not increase the thermoregulatory efficiency, i.e. regardless of the higher electrical activity oxygen consumption per unit body weight was less on the 12th day in comparison with that recorded on the second day.

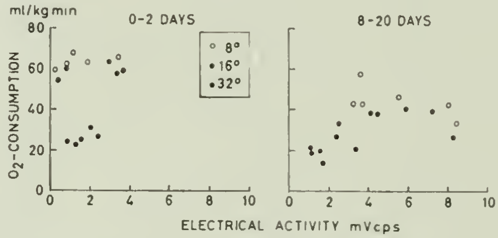

Fig. 5. Mean electrical activity and oxygen consumption of guinea pigs in relation to age and environmental temperature. Each point represents the mean oxygen consumption and electrical activity over a period of one hour (see text)

Figure 4 illustrates the gradual enhancement of electrical activity, occurring during the first three weeks of life.

All the results obtained from a group of 5 guinea pigs, which were studied on several occasions during the first weeks of life, are computed in the diagram shown in Fig. 5. Electrical activity, as measured at the 3 test temperatures, is plotted against the corresponding O_2-consumption. In young animals (0 to 2 days of age) wide variations of oxygen consumption are not accompanied by variations of the electrical activity whereas later on day 8 to 20 a positive correlation between O_2-consumption and electrical activity could be recognized.

Effects of Hexamethonium-Bromide

Chemical thermogenesis can be blocked at the efferent sympathetic fibers running within the adventitia of the arteries to the muscles (Freund and Jansen 1923), or by ganglionic blockage produced by hexamethonium-bromide (Hsieh, Carlson and Gray, 1957). It has also been shown that oxygen consumption can be markedly raised by norepinephrine in cold-adapted rats (Hsieh and Carlson, 1957), in newborn kittens (Moore and Underwood, 1962; Scopes and Tizard, 1963), and in newborn babies (Karlberg, Moore and Oliver, 1962). Thus, there is some evidence for the assumption that chemical thermogenesis is mediated by norepinephrine, as has been suggested by Hsieh, Carlson and Gray (1957).

Hexamethonium-bromide has been used in our studies as a tool for a rough estimate of the proportional contribution of chemical thermogenesis to the total heat production in relation to age.

Oxygen consumption was markedly reduced in young guinea pigs following the application of hexamethonium-bromide, (Fig. 6); with increasing age the effect became gradually less.

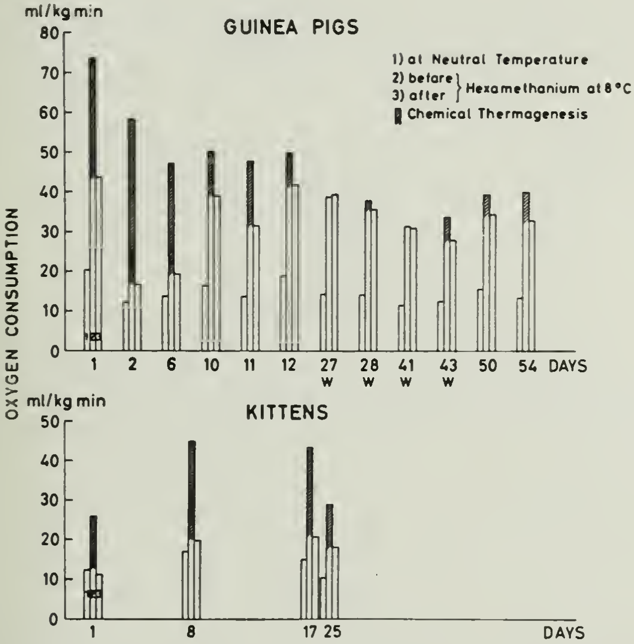

Fig. 6. The effect of hexamethonium-bromide on oxygen consumption rate in guinea pigs and kittens in a cold environment (guinea pigs: 8° C; 1-day-old kitten: 26°; other kittens: 18° C). For comparison minimal oxygen consumption at neutral temperature is plotted (first column). W = animals had been maintained at 30° C from birth

Surprisingly, one 1-day-old animal (Fig. 7) began to shiver while O_2-consumption was dropping under the influence of hexamethonium-bromide. It must be concluded from this that the mechanism of shivering was already present at the time of birth but was not set in motion under normal conditions.

In 2 out of 4 animals which had been maintained from birth at an environmental temperature of 32° C, oxygen consumption remained entirely uninfluenced by hexamethonium-bromide, even at a dose rate of 35 mg/kg. This indicated that chemical thermogenesis had been fully replaced by shivering heat production (Figs. 6 and 8). The remainder of the animals had been kept from birth at the normal temperature of the animal house, i.e. at 12 to 16° C. In the latter case a slight reduction of oxygen consumption could still be evoked at the age of 50 and 54 days (Fig. 6.).

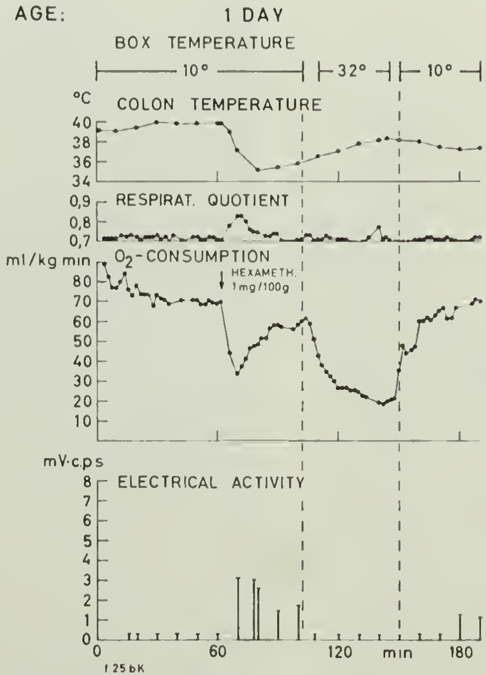

Fig. 7. The effect of hexamethonium-bromide on a 1-day-old guinea pig. Note that electrical activity increased while oxygen consumption dropped following the injection of the drug.

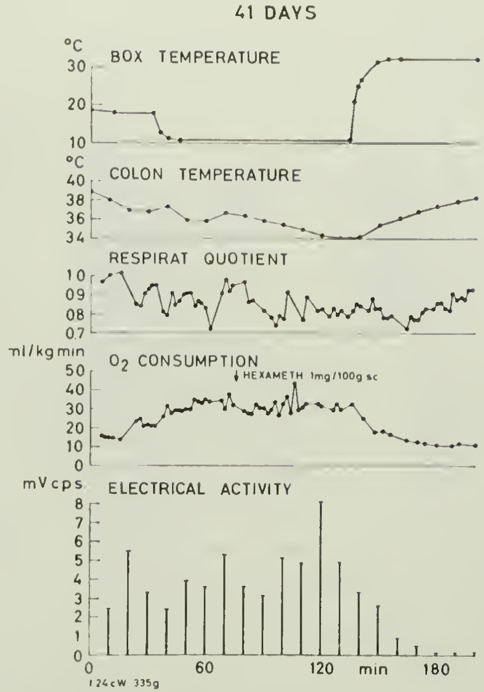

Fig. 8. Experiment on a 41-day-old guinea pig which had been kept at 32° C from birth. Note that oxygen consumption was practically unaffected by the injection of hexamethonium-bromide

Hexamethonium-effects in Kittens .

Four kittens, 1-, 8-, 17- and 25-day old, were examined. As illustrated by Fig. 7 oxygen consumption was reduced to the basal level in the one day old kitten. In the 7-day-old kitten, which displayed slight shivering, and in the 17- and 25-day-old animals, which showed more vigorous shivering, O_2-consumption was less and less reduced. These findings are in agreement with previous studies by Moore and Underwood (1962).

As is seen from Fig. 8 the replacement of chemical thermogenesis occurred less rapidly in the cat. This would be in accordance with the well known fact that guinea pigs are born in a more mature state than kittens.

DISCUSSION

The results of the present study provide evidence that in newborn guinea pigs and kittens the elevation of heat production in a cool environment is brought about by so-called chemical thermogenesis. In the course of the first weeks of life chemical thermogenesis is replaced to a considerable amount by shivering heat production. From a quantitative evaluation of the results it can be concluded that the shivering mechanism is less effective than chemical thermogenesis. Even with vigorous shivering in older guinea pigs the level of O_2-consumption reached does not exceed 30 to 40 ml/kg/min (Fig. 8). Heat production corresponding to this degree of O_2-consumption is sufficient to counterbalance heat loss in the larger guinea pigs exposed to an environmental temperature of 8° C (Fig. 5). Oxygen uptake in the order of 50–70 ml/kg/min was required, however, to compensate for the relatively larger heat loss of small newborn animals exposed to the same environmental conditions (Figs. 5 and 6). Obviously, the high heat production necessary for small newborn guinea pigs could only be provided by the more effective chemical thermogenesis.

The unclothed newborn baby is able to keep its body temperature at a level of 37° C when it is exposed to an environmental temperature of 23° C. Oxygen consumption has been found to be increased by 100 to 200 per cent over basal rate under such conditions, and no visible shivering could be observed (Brück, 1961). Thus, it can be assumed that in newborn babies as well as in guinea pigs and kittens chemical thermogenesis is prevalent during the early stage of life.

In the light of the studies presented the development of chemical thermogenesis in the course of cold-adaptation does not appear to represent the formation of an entirely new mechanism; it is rather to be thought of as a re-manifestation of a mechanism that has already been in operation during an earlier period of life.

The fact that chemical thermogenesis is well developed in newborn subjects which have never experienced cold environmental conditions requires consideration in a concept of the basic mechanism of cold-adaptation.

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CENTRAL NERVOUS MECHANISMS OF ADAPTATION

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Abstract – Physiological adjustments to heat and cold are integrated responses, largely controlled by the brain. The principal physiological mechanism that brings about acclimatization may be habituation, a non-specific adaptive process which allows the setting up of inhibitory pathways and a lessening of arousal, so that a given stimulus gradually produces a lesser response and fewer sensations.

Zusammenfassung – Anpassungen an Kälte und Hitze sind einheitliche Reaktionen, die zum grossen Teil vom Gehirn kontrolliert sind. Der wichtigste Akklimatisationsmechanismus ist wahrscheinlich die Gewöhnung, ein nichtspezifischer Anpassungsprozess, bei dem ein gegebener Stimulus allmählich eine kleinere Reaktion und weniger Wahrnehmung bewirkt.

Résumé – Les adaptations physiologiques au froid et à la chaleur constituent une réponse intégrée commandée en grande partie par le cerveau. Le principal mécanisme physiologique de l'acclimatation est probablement l'accoutumance, processus d'adaptation non-spécifique comportant la mise en jeu de circuits inhibiteurs ainsi qu'un affaiblissement de l'activation, si bien que, peu à peu, un stimulus donné provoque des réactions de plus en plus faibles et des sensations de moins en moins nombreuses.

It is a simple fact, though it is often forgotten, that the immediate result of any environmental change is the setting up of reflexes. Acclimatization is often a modification of such reflexes. Reflexes are automatic responses to specific stimuli depending on pathways through the nervous system. (Only so-called axon reflexes exclude the central nervous system, and they are not very important). The most important physiological influences which modify reflexes are impulses arising in the central nervous system. It follows that the scientific study of environmental adaptation must first and foremost consider stimuli, responses, and mechanisms that can modify responses.

The basic processes of physiological adaptation to heat and cold are unlikely to be situated in the peripheral nerves because these are not specific enough (Hensel, 1961, 1966). It is known that some environmental adaptations take place outside the nervous system, for example, variations of endocrine secretions or of subcutaneous fat, but this cannot explain all the phenomena observed. This leaves the central nervous system as the most likely site of these adaptations. There is much evidence that this is true, and the main interest is no longer to find out whether the central nervous system is involved but which of its parts have any effect.

It is wise, however, not to place too much emphasis on one or other region of the brain, as there are so many connections between its different areas that it is difficult for any one group of cells to act wholly independently from others in an intact brain. But it is probably true to say that the cerebral cortex plays a predominant part in adaptation to heat and to cold.

DEFINITIONS

Only those words will be defined and discussed here which are frequently misused or misunderstood.

Adaptation means any process, whether it is quick or slow, whereby a biological system or any of its parts becomes better able to exercise its normal functions or to survive. An adaptation can take place within seconds, for example when a nerve fibre ceases to conduct stimuli after a short period; it can take thousands of years, as in the evolution of some protective mechanism in a species. It can be a reflex, as for example dark adaptation of the pupil, or involve much conscious effort, as in adaptation of man to a new social environment. It can include learning, conditioning and habituation.

Acclimatization means comparatively slow and reversible adaptations to meteorological environment, which are not reflexes. It usually appears or disappears in the course of hours or days or longer periods. Acclimatization is an acquired ability to modify responses to environmental stimuli. Obviously, it can only be present with regard to stimuli which have been recently and frequently experienced. The stimuli and responses must therefore be defined. The underlying mechanisms can be the same even if the environmental stimuli differ, and for this reason it does not help to use special words, like "acclimation" for slow environmental adaptations in rooms. It is necessary to define the environmental stimuli and to describe responses.

Learning, conditioning and habituation are the processes whereby the central nervous system can modify responses to stimuli which have been previously experienced. They all presuppose the ability to recognize certain stimuli and they are predominantly brought about by the cerebral cortex.

In learning new responses are acquired or existing responses undergo qualitative and quantitative changes. In conditioning a response remains essentially unchanged but it can be produced by a new stimulus. In habituation the stimulus is unchanged but the response undergoes a quantitative change, usually it diminishes or disappears.

Arousal is a process whereby incoming impulses activate certain functions of the brain. Arousal is mediated by impulses that are likely to enhance or inhibit the survival or the well-being of an organism. Awards and punishments cause arousal. This can obviously reinforce learning, conditioning and habituation. Arousal itself can be modified by learning, conditioning and habituation.

THE PHYSIOLOGICAL BASIS OF THERMAL ADAPTATION

The following will deal mainly with responses to heat and cold because much of the experimental work which will be discussed was done with thermal stimuli, but many of the conclusions probably apply to high altitudes as well.

The physiological process which is the most frequently used to make thermal adjustments is a change of the peripheral blood flow. The stimuli which alter the peripheral blood flow are not only thermal ones but they can also be emotional. For example fear can cause superficial vasoconstriction and divert blood from the skin to the muscles, excessive emotion can cause fainting by allowing too much blood to flow into the muscles, some emotions cause vasodilation of the face, and so forth. Other heat regulating responses, such as sweating, or panting, or shivering, can also be related to emotional stimuli. Thus there is a close connection between heat regulation and emotion. The pathways are mainly nervous and also mediated through body fluids, but there is no need to consider these here.

In the primitive state physiological responses to emotions are often an advantage. It is an interesting phenomenon, for example, that females and the young are likely to faint in the presence of danger, thus avoiding attack by being immobile, while the more expendable adult males tend to develop pallor, panting, acceleration of the heart and raised blood pressure, all of which improves the oxygen supply to the heart and muscles and makes people fit to fight. In experiments emotional factors can confuse the results, but they can also show how some control mechanisms work.

Investigations of this began ten years ago when a series of experiments showed that changes of interest could alter the responses of people to identical stimuli, that responses could depend not only on the nature of the stimulus but also on what the experimental volunteers expected the stimulus to be, and that if all conditions were perfectly standardized the responses to the same stimulus gradually diminished due to habituation (Glaser, 1953, 1954; Glaser and Whittow, 1954). These experiments were not concerned with temperature regulation, but subsequent experiments showed that all this was equally true with regard to localized thermal stimuli (Glaser and Whittow, 1957; Glaser, Hall and Whittow, 1959) and with regard to the activities of the sweat glands (Glaser and Lee, 1959). A look at earlier results, moreover, suggested that the processes present during acclimatization to heat and cold may have had similar characteristics (Glaser, 1949).

Habituation soon emerged as a basic central nervous mechanism which might play a part in all kinds of adaptations (Glaser and Whittow, 1953) and especially in acclimatization (Glaser, 1957). Subsequently it was found possible to adapt one hand, but not the other, to heat and to cold at the same time, so that the pain, the rise of heart rate and the rise of blood pressure which accompany severe cooling and warming of the hand were all abolished, and it was possible to maintain this adaptation for a few weeks; it was also found that this adaptation could be cancelled out by emotional stimuli, the adaptation reappearing when the volunteer's mind was at peace again (Glaser, Hall and Whittow, 1959). This seemed to explain how acclimatization might be brought about. If adaptation to heat and to cold could be localized in one hand, it had to be caused either within that hand, or within the peripheral nerve supply of that hand, or in the cerebral hemispheres which control one side of the body. No other region could exercise strictly unilateral control of the body. Tests of the skin temperature and blood flow of the hand showed that there was no permanent underlying change of the hand blood flow, and it would have needed several indefensible assumptions to suggest that any mechanism within the hand itself might cause simultaneous heat and cold adaptation of one hand, but not of the other. Everything thus pointed to the cerebral hemispheres. It is known that the brain can store diverse information and that habituation to different stimuli is possible at the same time; but it seems unlikely that there could be opposing metabolic adjustments, or that opposing changes could be present at the same time, in the nerves of the hands. The part played by emotion seemed to confirm that the brain was involved.

It remained necessary to find out whether these localized adaptations to heat and cold were really related to acclimatization of the whole body and to find out what part of the cerebral hemispheres might have any effect. This was done in two separate sets of experiments.

The relationship of localized adaptation to acclimatization was demonstrated in an experiment in which 15 men were simultaneously acclimatized to heat and to cold by spending 3 hr daily at 3° C and 3 hr daily at 35° C for 9 out of 11 days (Glaser and Shephard, 1963). There was evidence of acclimatization to both environments, consisting of smaller changes of temperature, lesser vasomotor responses, and less discomfort with a given amount of cooling and warming. This was not only so when the whole body was cooled and warmed; responses from cooling or warming of a hand were also smaller at the end of the experiment. In other words, the responses to localized hot and cold stimuli could be inhibited after acclimatization responses of the whole body.

The brain areas which are primarily involved were first identified in animals. It was found possible to test rats by cooling their tails. This caused an increase of the rat's heart rate which could be electronically recorded (Glaser, Griffin and Knight, 1960). If the rat's tail was so cooled several times daily for a number of days, the response of the heart rate diminished or disappeared; this was obviously habituation, and it closely resembled habituation to cooling or warming of the hand.

If a small bilateral lesion was placed in the frontal area of the rat's cerebral cortex, then the response to cooling of the tail was still present, but habituation did not take place. Lesions on one side of the frontal region did not prevent habituation, but this is to be expected because the rat's brain is not divided into hemispheres and because the rat's tail is connected with both sides of the central nervous system. If a control lesion was placed elsewhere in the cerebral cortex, the rats habituated normally (Glaser and Griffin, 1961).

Confirmation of this has now been obtained in man (Griffin, 1963). Mental patients who have had leukotomies (which isolate the frontal areas of their brains), habituate more slowly to cooling or warming of their hands than normal people. Mental patients who have had no leukotomies behave more like normal controls.

There can be little doubt, then, that habituation to heat and cold depends at least to some extent on the cerebral cortex and that habituation is a basic mechanism of acclimatization to heat and cold. But this is not the whole story.

FURTHER ASPECTS OF THE PROBLEM

Other Cerebral Mechanisms

It has already been said above that some processes of acclimatization are not at all, or not wholly, central nervous. It must be added that habituation is not wholly dependent on the cerebral cortex, nor is it the only cerebral mechanism involved.

In the present state of knowledge, there is a danger of overestimating the part played by arousal but it would be an equal mistake to underestimate it. When an impulse reaches the central nervous system it is distributed to a number of areas, one of which is the ascending reticular formation. The reticular formation sorts out those impulses which by heredity or by experience appear relevant to survival or well-being of the organism, and it alerts the cerebral cortex whenever an impulse is potentially beneficial or harmful. The opposite effect is equally important because the suppression of irrelevant impulses allows the central nervous system to respond all the more when relevant ones are applied. Habituation is the process whereby irrelevant stimuli are suppressed; but the temporary loss of habituation at moments of stress (see above) allows greater alerting when necessary. There is much evidence that brain areas other than the cerebral cortex play a part in habituation, (see Hernandez-Peon and Brust-Carmona, 1961; Kozak, Macfarlane and Westerman, 1962), but it is probable that the frontal areas of the cortex have an overriding role.

Learning and conditioning should not be forgotten. According to the above definitions, learning need not be a conscious process. But both conscious and unconscious learning must play a part in acclimatization. For example, in the presence of heat, movements become slower, the shade is sought, food intakes are changed, water intakes are varied, and all this must help the acclimatized. Conditioning will further reinforce acclimatization. Thus acclimatized people can shiver or sweat when they enter a cold or hot room before there has been adequate body cooling, perhaps through associated non-thermal stimuli, and such conditioned reflexes are bound to be present whenever there is acclimatization. Habituation is the negative side of acclimatization whereby excessive responses to heat or cold are prevented; learning and conditioning positively enhance those responses which are beneficial.

Effects of Drugs

Learning, conditioning and habituation can be influenced by drugs (Glaser, 1962) and changes of temperature can modify pharmacological actions (see Fuhrman, 1963). Minerals and vitamins are already widely used in extremes of climate, though their value is sometimes small (Ladell, 1947; Glaser and Livett, 1957). It is too soon to tell whether it will ever be possible to help or hinder environmental adaptations by giving drugs, but interesting possibilities are opened up by the facts that the brain influences adaptations and that drugs influence the brain.

CONCLUSION

One of man's principal characteristics is his brain, which is far more complex and effective than that of any animal. One of man's principal advantages is his ability to live anywhere on earth, perhaps even outside it. This ability is partly due to the fact that man can learn and deduct from observation, more so than any animal. But it seems possible that his better brain also gives him an advantage in unconscious central nervous mechanisms of adaptation.

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THE TIME FACTOR IN ADAPTATION

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Abstract – The time factor must be taken into consideration not only in regard to the kinetics of adaptive reactions, but also in the characterization of the stressors and their relations to the internal time scheme of the organism. From a comparison of the minimum time of exposure needed for the initiation of adaptive reactions to various stressors it is concluded that the more directly the stimulus is able to change the internal milieu of the organism, the shorter the required duration of exposure is. When comparing the natural diurnal variation of different stressors with the temporal course of the stimuli in laboratory experiments it is understandable that the disturbance of normal synchronization of diurnal rhythms causes significant differences in natural and experimental adaptation. It is shown that the normal synchronization of the diurnal rhythm in itself means a phasal adaptation to the external temperature cycle. The mechanism of this adaptation is non-specific. By increasing the amplitude it can obviously be used for adaptation to both heat and cold. Hibernation can be regarded as an extreme seasonal form of temperature adaptation through synchronization. Concepts of adaptation always depend upon the length of the observation period. The developmental kinetics and of adaptive compensations the specific sequences in which they appear, are largely determined by the characteristics of the organism. With the chronological progress of the adaptive process, the compensatory reactions become more and more stable, specific, and economical. It is quite possible that the time course of adaptation is divided into phases by a basic periodicity of vegetative regulation, whereby ergotropic compensations and trophotropic adaptive mechanisms are arranged alternately. Adaptive abilities are also influenced by age as well as by the phases of long-term biological rhythms.

Zusammenfassung – Der Zeitfaktor ist nicht nur bei der Kinetik adaptiver Reaktionen, sondern auch bei der Beurteilung des Stressors und seiner Beziehungen zur zeitlichen Struktur des Organismus zu berücksichtigen. Die Expositionszeiten können umso kürzer sein, je schneller und direkter der Stressor das innere Milieu des Organismus stört. Die normale Synchronisation der Tagesrhythmik ist eine phasengerechte Anpassung an den äusseren Temperaturzyklus. Dieser Mechanismus ist unspezifisch und kann durch Amplitudensteigerung sowohl für Kälte- als auch für Hitzeadaptation wirksamer gemacht werden. Hibernation kann als Extremfall einer Adaptation durch Synchronisation aufgefasst werden. Konzepte der Adaptation sind von der Dauer der zugrundeliegenden Beobachtungen mitbestimmt. Die Entwicklungskinetik sowie die charakteristische Sequenz adaptiver Kompensationen ist im Wesentlichen durch Eigenschaften des Organismus festgelegt. Nerval gesteuerte Kompensationen stehen schneller zur Verfügung als hormonale und trophische. Gemeinsam ist allen Sequenzen, dass die Kompensationen immer stabiler, spezifischer und ökonomischer werden. Dadurch können die meisten der initial mitreagierenden Funktionen entlastet werden und normalisieren. Es ist wahrscheinlich, dass der zeitliche

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Verlauf der Adaptate durch einen basalen periodischen Prozess der vegetativen Regulation in Phasen gegliedert wird, wobei ergotrope spezifische und trophotrope unspezifische Mechanismen alternieren. Die adaptiven Leistungen werden vom Lebensalter sowie von den Phasen der langwelligen biologischen Rhythmen beeinflusst.

Résumé – Le facteur temps ne doit pas être pris en considération uniquement dans les réactions d'adaptation dont le mouvement est visible, mais aussi dans l'évaluation des éléments nuisibles et de leurs relations aux modifications de structure de l'organisme. Les temps d'exposition peuvent être d'autant plus brefs que l'élément nuisible perturbe rapidement et directement le milieu interne de l'organisme. La synchronisation normale au rythme nycthéméral est une adaptation des phases internes au cycle extérieur de température. Ce mécanisme n'est pas spécifique et peut être rendu plus actif par l'adaptation aussi bien au froid qu'au chaud par simple augmentation des amplitudes. L'hibernation peut être considérée comme un cas extrême de l'adaptation par synchronisation. Les critères d'adaptation sont en outre conditionnés pour nous par la durée des observations de base. L'évolution du développement tout comme la période caractéristique des compensations à l'adaptation est déterminée principalement par les particularités propres à l'organisme. Les compensations provoquées par le système nerveux sont plus rapides que celles obtenues par voie hormonale ou trophique. Un fait commun à tous les phénomènes de compensation c'est qu'ils deviennent de plus en plus stables et économiques. De ce fait, la plupart des fonctions organiques touchées au début peuvent être déchargées et normalisées. Il est probable que la succession dans le temps des conditions d'adaptation est divisée en phases périodiques de régularisation végétative. Dans ce cas, les mécanismes ergotropes spécifiques alternent avec d'autres non spécifiques, mais trophotropes. Les processus d'adaptation sont influencés par l'âge des individus et par les phases des rythmes biologiques lents.

THIS paper presents a survey of the problem of adaptation as a function of time. Adolph (1956, 1962) is the only one so far who has made a systematic attempt to determine the part played by the time factor in the mechanism of adaptive processes. Otherwise, the element of time has been treated as a "stepchild of adaptation research" (Jungmann, 1962). This is true in regard to the inadequate length of most observation periods, and also to the sometimes excessively long intervals between observations. In addition, not enough attention has been paid to the fact that time as a periodic structure is an integral component of biological organization itself, and that it is co-ordinated with the periodicity of environmental conditions (cf. Hildebrandt, 1962a).

For this reason, our discussion must deal not only with the time course of adaptive reactions, but also with the time characteristics of the initiating stressor and the effects produced in the internal time scheme of the organism. These various problems can, of course, be dealt with only in general terms in this short introduction. Moreover, I shall limit myself largely to the subject of temperature and altitude adaptation, and for purposes of comparison shall refer to muscle training as an example of local adaptation. These stressor qualities are the ones which have been studied most extensively so far, especially in their effect on human beings.

THE TIME FACTOR IN STIMULATION AND EXPOSURE

1. Duration of Stimulation and Initiation of Adaptation

Adaptive modifications in the organism presuppose a stimulus of unusual intensity or unusual quality. The earliest manifestations are observed following a high-intensity stimulus. However, they depend on a certain duration of the stimulus; this duration varies considerably, depending on the quality of the stimulus. For instance, if rats are exposed to cold air, significant adaptive changes appear after approximately 48 hr (Fregly, 1953; Adolph, 1956). This time lapse decreases to 6 hr only in the case of whole-body cooling, which rapidly causes central hypothermia (Adolph, 1956).

In the case of oxygen deficiency or low pressure, the minimum exposure time is shorter; only a few minutes to a few hours are needed to set off adaptive processes (Fregly, 1954; cf. Adolph, 1956).

The necessary duration of stimulation becomes extremely short in muscular strength training. Müller and Hettinger (1953, 1955) have shown that a single tensing of a muscle for a few seconds leads to an optimum hypertrophy and increase in strength for the following seven days.

Certain adaptive mechanisms are completely developed by one single exposure, while others obviously require repeated exposure before they appear. In his comparison of stimulus qualities, Adolph (1956) found that a single water, salt, or glucose stress produced maximum adaptive effects, whereas hypoxia and cold did not cause any changes until after two to three exposures.

From these findings we can conclude that the more directly the stimulus is able to change the internal milieu of the organism, the shorter the required duration of exposure is. Adaptations to cold require the longest period of exposure, since there is a certain latency in central cooling.

2. The Time Factor in Exposure

In order to evaluate properly the importance of the time factor in exposure, it is useful, as has already been shown by Schaefer (1962), to begin by considering the natural environmental stimuli as a function of time, even though their effects are sometimes modified by the reaction of the organism.

Under constant solar radiation, the air temperature and "frigorimeter" rate showed a daily rhythm of considerable amplitude. Compared with the radiation rhythm there is a phase shift of approximately three hours, which is also true of the daily rhythm of body temperature in the organisms (Fig. 1). In contrast, the undisturbed daily course of atmospheric pressure is relatively constant; in particular, it has only a minimum periodic component.

In contrast to natural altitude change (Fig. 2), adaptation to simulated altitude in the laboratory by means of hypoxia or low pressure is usually produced with intermittent exposure, mainly because otherwise the animals refuse to eat, especially if the pressure is markedly low (Mercker and Schneider, 1949; Vest and Wang, 1950). Here the scale of methods ranges from a few seconds of exposure daily to allday exposure with one hour of interruption. Such a procedure appeared to be

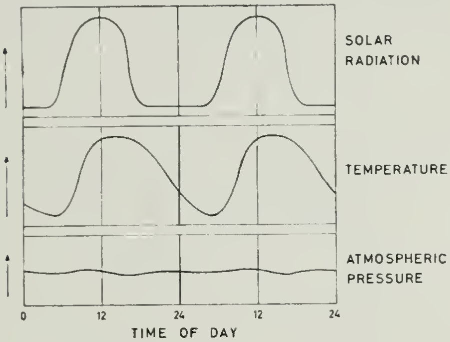

FIG. 1. Mean daily course of solar radiation, temperature, and atmospheric pressure. (Data from Becker, 1962). The amplitude relationship between temperature and atmospheric pressure was obtained from the relationship between the two altitude gradients

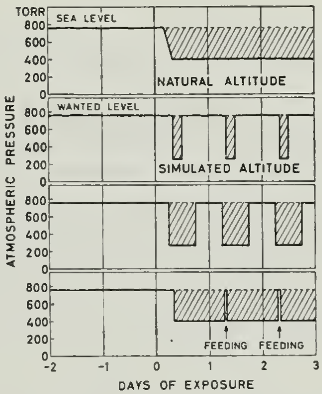

FIG. 2. Time course of atmospheric pressure during change to natural altitude and during intermittent exposure to low pressure in the laboratory (schematic)

justified, since if the intensity of the stimulus and the duration of exposure are systematically varied, the development of rapidly appearing modifications (e.g. increase in the hematocrit ratio, or increase in erythrocytes) is determined mainly by the product of intensity, duration, and frequency of exposure (Altland and Highman, 1951; Adolph, 1956; cf. Stickney and Van Liere, 1953). Thus the difference in comparison with continuous altitude effect would be merely a quantitative problem.

However, in animal experiments it has always been found that intermittent jumps in pressure are more stressful, and that they produce a worse general condition, greater loss of weight, central lesions, and a higher mortality rate than do comparable continuous exposures (Anthony *et al.*, 1959; Stickney and Van Liere,

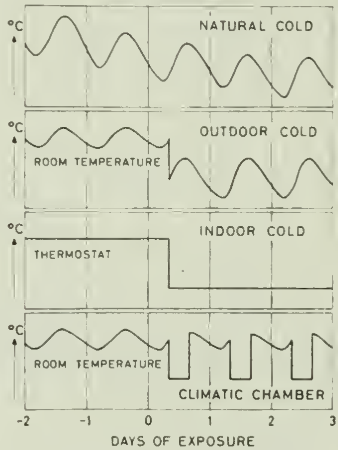

FIG. 3. Time course of air temperature during natural cooling and during experimental exposure to cold under various conditions (schematic)

1953). This agrees, by the way, with the observations which have been made in mountain-railway personnel, who are exposed to frequent and rapid changes in altitude, which they are usually unable to withstand indefinitely.

However, the most important difference was found after intermittent exposure to simulated altitude: here, no increase in myoglobin could be demonstrated in the skeletal muscle, although in exposure to natural altitude this increase is an important and very stable adaptive modification in the tissue. (For references, see Hensel and Hildebrandt, 1964b). However, it is not an early form of adaptation, but rather one of the effects of advanced adaptation, most of which have a particularly economical effect.

In adaptation to cold, the greatest difference between natural and experimental conditions is found in regard to the time factor (Fig. 3). With natural cooling, e.g. of a seasonal nature, the daily temperature rhythm gradually sinks to a lower level, whereas in the laboratory the set point of climatic chambers is usually adjusted to a low level. This method is sometimes used intermittently, e.g. in climatic-chamber experiments with human subjects. Davis (1961) exposed his test persons 8 hr/day. However, in work-rooms and animal stalls the daily air temperature may take a rhythmic course, although with a much smaller amplitude.

It has been known for some time that animals living in a natural state, with seasonal adaptation to cold, differ in various ways from experimental animals which have adapted to laboratory conditions. However, it was not until the recent systematic studies of Heroux *et al.* that conclusive evidence was produced on significant qualitative differences in cold adaptation which are caused by the fluctuating temperature conditions in the outdoor environment. Under indoor conditions the animals do develop similar degrees of resistance to cold and metabolic compensation, but this is accompanied by marked hypertrophy of the cardiac muscle and endocrine organs, as well as by loss of weight (Heroux and Schönbaum, 1959; Heroux and Campbell, 1959). In particular, there is no improvement in peripheral insulation through fur growth or other peripheral adjustments (Heroux, 1959, 1961; Heroux *et al.*, 1959). Tests with intermittent indoor exposure also lead to adaptive reactions of the indoor type (Heroux, 1960).

Thus, in adaptation to cold under artificial exposure conditions, the symptoms of a general stress effect are predominant, whereas there is no formation of the particularly specific, economical, and stable signs of advanced adaptation in the peripheral tissues.

Since under laboratory conditions either the natural time regimen of the environmental stimuli is lacking, or there are additional periodic stimuli, we must look more closely at the possible significance of the natural synchronization of biological rhythm with the environmental rhythm in regard to adaptation.

3. *Synchronization*

Under natural conditions, the rhythmic functions of organisms are synchronized with the daily and seasonal environmental rhythms by means of periodic environmental stimuli. (For references, see Hildebrandt, 1962a; Aschoff, 1963). Light stimulus plays a dominant part as a synchronizer, while in warm-blooded animals the temperature is less important. In the daily rhythm, the synchronization mechanism can be thought of as follows (Fig. 4): the morning light stress causes a periodically damped reaction, the steepest ergotropic phase of which is coupled with the same phase of the endogenous component. The natural daily curves, e.g. pulse rate, often show clearly that these two components are superimposed (Hildebrandt. 1962).

The organism is able to follow changes in frequency or phase shifts in the synchronizer only within certain limits, and in each case there is a temporary decrease in the amplitude of the biological rhythms. Figure 5 shows the effect of a 12-hr phase shift in light-dark rhythm on the activity periods of chaffinches, according to experiments made by Aschoff (1960). Since the endogenous rhythm can follow only at a speed of one to two hours per day (Aschoff and Wever, 1963), time adaptation to the new synchronizer regimen takes at least 6 to 10 days.

Natural fluctuations in atmospheric pressure cannot be considered as synchronizers, but it appears to be quite possible that the periodic stress effect of intermittent exposure to low pressure competes with the normal synchronizers and causes disturbances in synchronization.

The adaptive significance of natural synchronization becomes especially evident in the case of temperature rhythm. Because of the natural phasal relationship

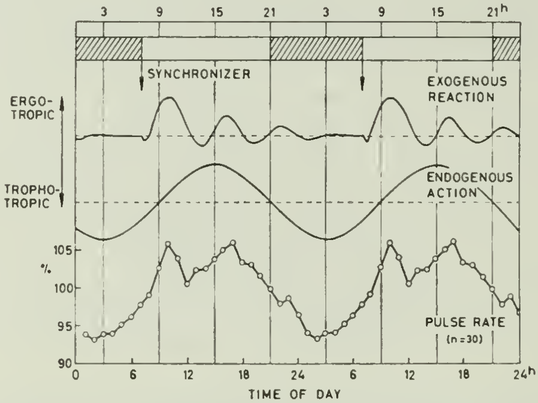

FIG. 4. Mean daily course of pulse rate (bottom curve) in 30 tests with hourly measurement, resulting from periodic reaction to synchronizer stimulus and an endogenous sinusoid component of daily rhythm. (According to Hildebrandt, 1962a)

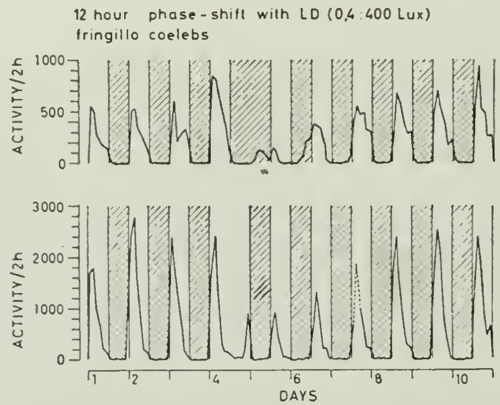

FIG. 5. Activity of chaffinch in alternating 12 hr of light and 12 hr of darkness. Phase shift of the synchronizer for 12 hr by doubling light-time (below) or dark-time (above). (From Aschoff, 1960)

between light-dark alternation and temperature variation, rises and falls in body temperature are, in an economical manner, approximately parallel to those in open-air temperature under synchronized conditions. Likewise, seasonal changes in fur insulation, which are demonstrably controlled by light rhythm, are purposeful only if they are properly synchronized.

The significance of a synchronized temperature rhythm can also be experimentally demonstrated in human beings (Fig. 6). Under constant environmental conditions, vasoconstrictor reactions to a cold test stimulus, as measured by the time required for rewarming, are considerably stronger and of greater duration when body temperature increases in the daily rhythm, e.g. between 3 and 15 hr, than during the afternoon phase of heat loss. Vice versa, the ability to sweat, as measured by forehead sweating after a hot test stimulus (drinking diaphoretic tea) is consider-

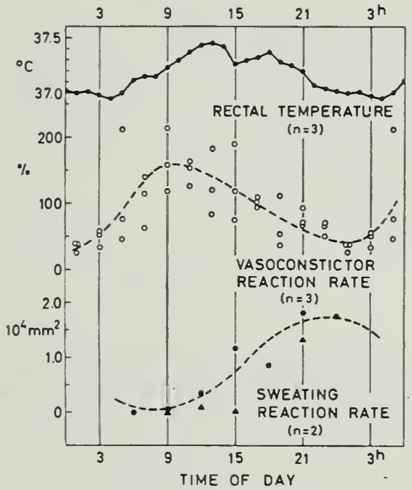

FIG. 6. Daily course of rectal temperature, duration of vasoconstrictor reaction after cold hand-bath, and planimetric magnitude of sweating reaction on the forehead after drinking diaphoretic tea. (Data from Hildebrandt *et al.*, 1954; Hildebrandt, 1957)

ably greater in the phase of decreasing body temperature than during the rewarming period of the daily rhythm. This means that during a rise in body temperature (i.e. in a synchronized state: when the outside temperature is also rising) the organism is less sensitive to heat, whereas during the phase of internal and external cooling it is more tolerant towards cold. It can also be demonstrated in human beings that any given degree of tolerance is dependent upon the steepness of the daily rhythmic phase (Hildebrandt, 1957).

Thus the normal synchronization of the daily rhythm in itself means a phasal adaptation to the external temperature cycle. The mechanism of this adaptation is non-specific; thus it can obviously be used for adaptation to both heat and cold.

According to the studies of Schmidt-Nielsen *et al.* (1957), a daily amplitude of around 1–2° C is found in the rectal temperature of camels during the winter (Fig. 7). In very hot weather, however, when no water is available and loss of heat through evaporation must be limited, a considerable increase, of up to more than

6° C, was found in the daily amplitude. Since body temperature here increases to more than 40° C, there must be a simultaneous increase of tolerance towards overheating. This example clearly shows the particularly economical effect of this adaptation.

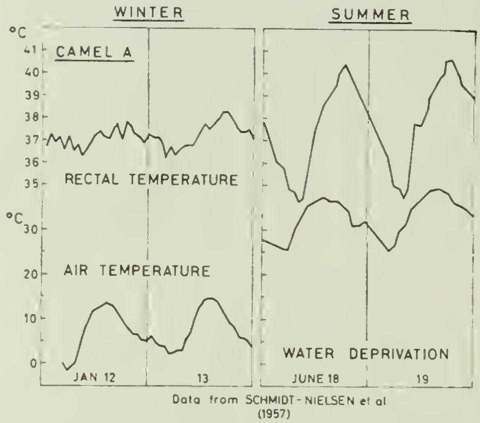

FIG. 7. Daily course of rectal temperature in a camel in winter and in summer. with water deprivation. (Data from Schmidt-Nielsen *et al.*, 1957)

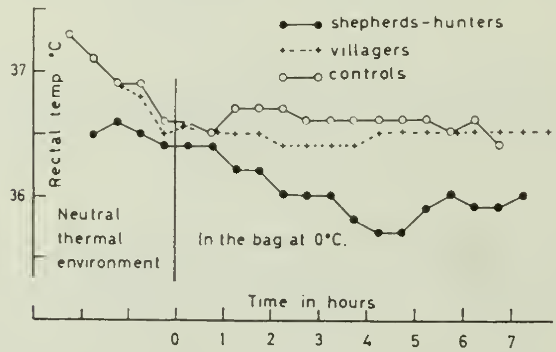

FIG. 8. Mean rectal temperature of Lapps, nomadic and villagers, and white control subjects when sleeping in the bag at 0° C (From Lange-Andersen *et al.*, 1960)

In human beings as well, an analogous mechanism appears to play a part, i.e. in individuals living in a primitive state who are completely exposed to the daily rhythm of the environmental conditions. So far, it has been shown in Australian aborigines (Scholander *et al.*, 1958; Hammel *et al.*, 1959) and in nomadic Lapps (Lange-Andersen *et al.*, 1960) (Fig. 8) that during night sleep outdoors under cold conditions, the rectal temperature sinks much lower than it does in white control persons. However, this has not been demonstrated in civilized Lapps or in African bushmen. In the former cases there is thus an increased tolerance, corresponding to the daily rhythmic phase. It remains to be determined whether these differences in the adaptional properties are related to different amplitudes in the environmental temperature rhythm to which they are accustomed.

In this connection we could think of hibernation as an extreme seasonal form of temperature adaptation through synchronization. Le Blanc has already pointed out a certain similarity between cold adaptation in man and hibernation. Because of the economical way in which they resist cold without losing their thermoregulatory power, hibernating animals, which can alter their desired daily temperature level according to the outside temperature, can be called "perfected homeotherms". Adaptation by means of synchronization and increase in amplitude is certainly one of the later, economical forms of adaptation. The effect is directly connected with natural synchronization, and thus is easily disturbed or suppressed by the usual experimental conditions. Since it is a non-specific mechanism which is equally effective in regard to both cold and heat, we must restudy the question of negative and positive cross-adaptation from this point of view.

THE TIME COURSE OF ADAPTATION

Adaptation following a change of environment is, strictly speaking, not a process with definite time limits, but rather an organic development, like life itself. The measurable degree of resistance can remain constant from a certain point of time onward, even though the underlying compensation mechanisms continue to develop. Prosser (1958) has shown that the adaptation mechanisms can be arranged in a certain chronological order: early responses during the first few minutes and hours, which usually subside with periodic damping; compensative reactions with metabolic, enzymatic, and morphological modifications, which develop in the course of days, weeks, and months. This is the limit of physiological adaptation in the individual, but over and above this there are adaptive mechanisms which cover much longer periods of time, such as non-genetic transmission, or even the selection of genetically adapted or mutated types, which requires evolutionary periods of time. In any case, it is important to know that our concept of adaptation always depends upon the length of our observation period.

The magnitude of the various adaptive reactions, which Adolph (1956) grouped together under the heading "adaptates", is mainly dependent upon the intensity of the stimulation. On the other hand, their developmental kinetics, and especially the sequence in which they appear, are largely determined by the characteristics of the organism. In its later stages, however, the continuation of the adaptation process appears to be a question of the specificity and time quality of the stressor as well.

The varying developmental kinetics of the individual adaptates is, among other things, a result of the varying time requirements of their initiation and control mechanisms (cf. Adolph, 1956; Yoshimura, 1960). Whereas nerve-controlled compensations, such as cold shivering, respiratory increase, and circulatory reactions, are rapidly available. modifications in tissue metabolism, which are mainly hormone-controlled, require a longer latency (e.g. non-shivering thermogenesis, enzyme induction, myoglobin formation, etc.). Barker and Klitgard (1952) have shown, for instance, that the metabolic increase following a single injection of thyroxin does not reach a maximum until the fourth day, and does not begin to subside until the sixth or seventh day. The induction of morphological responses probably requires an even longer latency in many cases.

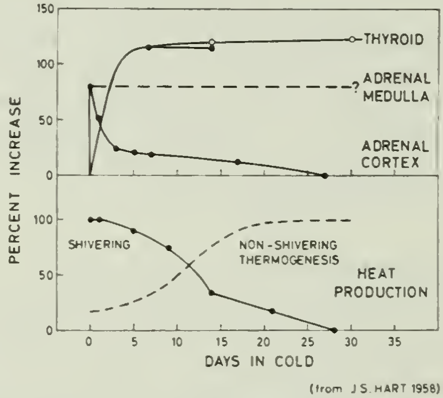

Fig. 9. Top, summary of endocrinological changes during acclimation to cold. Bottom, shivering and heat production through non-shivering thermogenesis. Ordinate, percentage increase over control rats not exposed to cold. (From Hart, 1958)

In the first stages of adaptation, the compensative reactions regress under continuing exposure; functions are thus normalized, and are superseded by other compensation mechanisms. If the period of observation is long enough, it has been found that adaptates which were previously considered to be permanent can also be normalized after months or even years (Le Blanc, 1963).

A number of characteristic adaptate sequences are known; in cold adaptation, e.g. cold shivering is superseded by the development of non-shivering thermogenesis (Fig. 9.) (cf. Hart, 1958, 1961; Smith and Hoijer, 1962). In the hormonal area, the initial reaction of the adrenal cortex is superseded by an increase in thyroid activity. In outdoor exposure, these adaptates are later replaced by an increase in insulation.

In altitude adaptation. respiration and circulation are the first to react, followed by water and mineral regulation. Then, according to Vannotti (1946) there is an increase in hemoglobin, followed by an increase in the myoglobin and cytochrome content of the tissue.

In strength training, an increase in strength first appears, followed by an increase in energy reserves. There also seems to be a characteristic sequence of modifications in speed training (cf. Hensel and Hildebrandt, 1964b).

All these sequences have one thing in common: with the chronological progress of the adaptation process, the compensative reactions become more and more stable, specific, and economical. The general functional reactions are superseded by tropho-morphological compensations in the tissue. Through this metamorphosis of the adaptates, a number of initially coreacting functions can be relieved and normalized (cf. Hensel and Hildebrandt, 1964a).

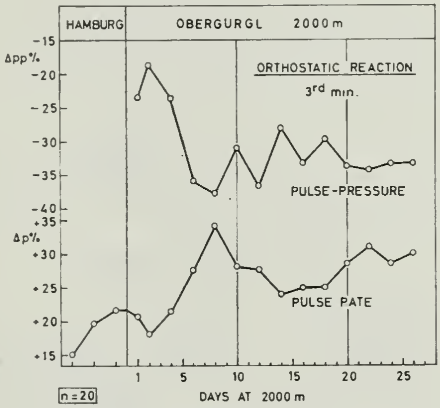

Fig. 10. Deviations in pulse pressure and pulse rate from repose values after standing for 3 min. Mean values for 20 students from Hamburg during a stay in Obergurgl (altitude 2000 m). (From Hildebrandt and Jungmann, 1962)

At the end of exposure, regression and normalization of the individual adaptates usually take place more slowly than did their formation; however, divergent observations have been made, in which de-adaptation progresses more rapidly. According to Adolph (1956), the time course of de-adaptation is independent of the developmental kinetics of the adaptates, but here too, contradictory evidence has been found: Müller and Hettinger (1954) have shown that the decrease in muscle power after the end of training takes place more or less gradually, in direct proportion to the gradualness with which the training was carried out.

But there is another question of much greater importance: whether, and to what extent, we can be sure of an unbroken constancy in the compensation effects during continuous exposure when various adaptates supersede one another. For this, the kinetics of regression and development would have to be perfectly co-ordinated with each other.

In therapeutic adaptation in human beings, it is known that the normalization of various functions takes place along a periodically damped course, and is interrupted by crises (acclimation crises) (Hildebrandt, 1962a, 1962b; Jungmann, 1962). The periods are usually of similar length, i.e. approximately 10 days. To illustrate this, Fig. 10 shows changes in the orthostatic regulation of the pulse rate and pulse-pressure at an altitude of 2000 m, as observed in healthy students (Hildebrandt and Jungmann, 1962). A damped subsiding of the periods is noticeable.

These phenomena have been studied more thoroughly in connection with balneo-therapeutic treatment in medium-altitude regions. Figure 11 shows a compilation of the data we obtained. Body temperature and circulatory functions

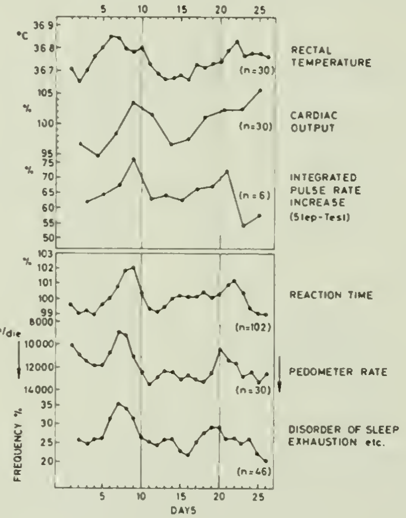

Fig. 11. Mean course of rectal temperature, cardiac output, integrated pulse-rate increase over repose value after step-test, reaction time to visual signal, daily pedometer rate, and frequency course of subjective disturbances during 4-week treatment in a medium-altitude spa. (Data from Gehlken *et. al.*, 1961; Hildebrandt and Steinke, 1962; Hildebrandt, 1962a, 1962b)

take a periodic course, with peaks in the vicinity of the tenth and twentieth days. In addition, a similar periodic course is found in the psychological reactions of the patients, as is shown by their reaction time, daily pedometer rate, and the frequency of their subjective complaints. This indicates a periodic pattern in the basic tonus of the vegetative system, with ergotropic critical phases and trophotropic normalization phases (cf. Hildebrandt, 1962a).

Betz and Wünnenberg (1963) recently succeeded in demonstrating a periodicity of similar magnitude in the course of adaptation in animal experiments with intermittent hypoxia. Figure 12 shows the normalization of brain blood-flow reactions in cats after repeated application of 10 per cent and 8 per cent O_2. In both cases, the regression of the reaction was interrupted by a renewed increase around the eighth to the tenth day. This shows that there must be a temporary weakening of other compensations.

Thus it is quite possible that the time course of adaptation is divided into phases by a basic periodicity of vegetative regulation. Here we must remember that in addition to the sequence of compensative reactions which are ergotropic in

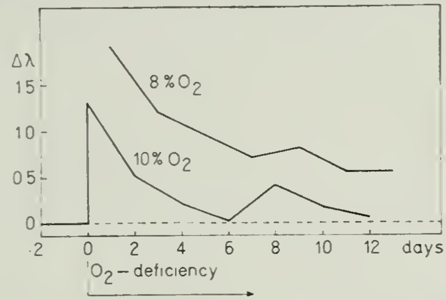

Fig. 12. Normalization of brain blood-flow reactions in cats after application of 10 per cent and 8 per cent O_2 for 4 hr every 2 days. (From Betz and Wünnenberg, 1963)

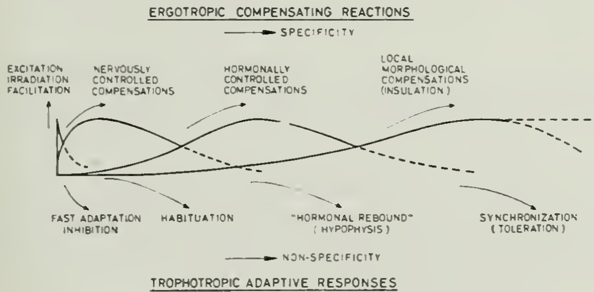

Fig. 13. Schematic representation of adaptive sequences. See text for fuller discussion

nature and become more and more specific, another sequence of trophotropic adaptive mechanisms, in the strict sense of the term, always takes place concomitantly (Fig. 13). However, these are completely non-specific, and participate in the damping and regression of the compensations. It is possible to think of these two competing sequences as being arranged alternately to form a periodic process.

BIOLOGICAL TIME PHASES AND ADAPTATION

If we place the time covered by an individual's entire life on the abscissa, we see that the particular age of the individual at a given point has a strong influence on his adaptive abilities; however, differences are found among the various stressors.

Hypoxia tolerance in newborn babies (Fazekas *et al.*, 1941) is greater than at any other time of life. In particular, the younger an individual is, the greater the vascularization effects in oxygen deficiency (Valdivia, 1958). This is also true of training for the purpose of increasing stamina (Petrén *et al.*, 1937).

In contrast, cold adaptation is but slightly developed in very young animals (Smith and Hoijer, 1962), although there is marked non-shivering thermogenesis in newborn animals. Brück (1963, 1964) recently showed that this is not replaced by

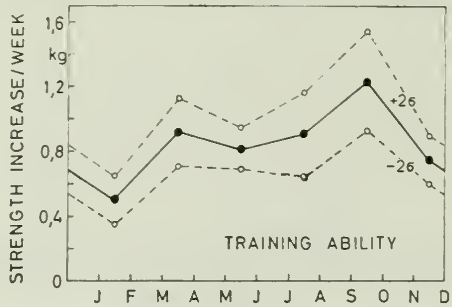

FIG. 14. Annual course of training ability in human skeletal muscles. (From Hettinger and Müller, 1955)

cold-shivering until a few days later. In rats, optimum cold adaptation is found between the sixth and sixteenth week of life. Older animals no longer show any reactions in tissue metabolism (Weiss, 1954); they tolerate greater loss of weight and react less acutely to the first exposure (Wertheimer and Bentor, 1957). In human beings, optimum adaptive ability is probably found between the fifteenth and thirty-fifth year of life (Hellpach, 1950). The training ability curve given by Hettinger (1958) also shows this maximum; however, it is more dependent upon age in men than it is in women.

In conclusion, we must not forget that adaptive ability is also influenced by the phases of long-term biological rhythms, e.g. by the generation cycle or the seasonal biological rhythm. As an incentive for further systematic studies in this field, I should like to show the annual course of training ability in human beings as found by Hettinger and Müller (1955) (Fig. 14).

I have certainly not touched upon all the aspects of the problem, but the points I have mentioned should be sufficient to show that the problem of the time factor must be dealt with on many different levels if we are to gain useful new concepts in regard to adaptation.

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ADAPTATION TO HYPOTHERMIA*

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Abstract Adult rats were cooled deeply twelve times during a four-week period. The thirteenth time they were cooled and kept at a body temperature of 22–25° C. Placed into a lever operated heat reinforcement apparatus they learned and performed for external heat after 74 min. None of the control rats (cooled only once) learned to use the heat reinforcement apparatus when their body temperature was 25° C or below.

Zusammenfassung — Ausgewachsene hypothermische Ratten mit einer Körpertemperatur zwischen 22 und 25° C waren unfähig, während einer Hypothermie zu lernen, einen Hebel zu betätigen, der eine Wärmequelle aktiviert und damit zur Wiedererwärmung führt. Nur Ratten, die zwölfmal einer gleichartigen Hypothermie ausgesetzt waren, lernten während einer dreizehnten Hypothermie innerhalb von 74 Minuten sich selbst zu erwärmen. Dieser Befund wird als neue Art von Adaptation an Hypothermie gedeutet.

Résumé — Pendant une période de quatre semaines, des rats adultes ont été refroidis profondément douze fois. Ils furent ensuite refroidis une treizième fois et la temperature de leur corps fut alors maintenue entre 22° et 25° C. Placés dans un appareil dont la chaleur est relevée par la pression de l'animal sur un levier, ils ont appris à exécuter ce mouvement en 74 minutes. Aucun des rats témoins dont la température du corps ne fut abaissée qu'une seule fois à 25° C ou moins n'a appris à se servir de l'appareil.

When a mammal is being cooled the activity of most of its body processes decreases. However, some processes increase initially but decline when hypothermia progresses further. An example of this is oxygen consumption, which in many mammals studied reaches a peak at a body temperature of 30° C (Popovic, 1959). Further lowering of the body temperature diminishes all physiological processes so that the critical temperature of cessation for various processes is found at different low body temperatures. For instance, the critical temperature for locomotion in rats is about 21° C, for lung ventilation is 13° C and for cardiac activity is 8° C (Adolph, 1959). Like other physiological activities the act vity of higher centers of the central nervous system is not abolished at a moderate hypothermia. It has been shown (Panuska and Popovic, 1963) that inexperienced rats, cooled to a body temperature of 29.6° C, are able to learn to use a simple heat reinforcement apparatus which will give them the possibility of rewarming to euthermia and

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surviving a situation in which otherwise they would perish. These rats begin to perform, i.e. to use the heat reinforcement apparatus, 48 min after being placed into the experimental chambers, much faster than euthermic rats in the same situation. It has been further found that rats will learn to perform for heat even in deeper hypothermia, the body temperature of 25° C being the lowest at which learning and performance was found (Panuska and Popovic, 1963). However, as hypothermia becomes deeper the duration of exposure as well as the number of necessary prior accidental reinforcements increase before performance begins. At a body temperature below 25° C rats fail to learn and to perform during a 3-hour experiment.

This hypothermia of 25° C and below, at which rats fail to learn and perform, was chosen to test the ability of "hypothermia adapted" rats to learn and perform. It was reasoned that animals which have been previously cooled on several occasions might stand deep hypothermia better and be in a better physiological state than rats which experience the same hypothermia for the first time. If this were true, then the hypothermia-adapted rats should be able to learn and perform at the same low body temperature at which control rats fail to do so. The present experiments are designed to test this hypothesis.

MATERIALS AND METHODS

Seven young white rats (Sprague-Dawley), 3 male and 4 female, were taken at the age of 10–20 days from three litters and were cooled by the Giaja confinement technique (1940) to a body temperature of 16° to 18° C and then left at room temperature to rewarm spontaneously to euthermia. Cooling by the same technique to the same body temperature was repeated three times per week for the next four weeks. At the thirteenth time the trunks of all rats (average body weight — 197 g) were clipped of hair and the animals cooled to a body temperature of $18.5 \pm 0.5°$ C. The rats were then taken from the cooling chambers and left to rewarm to 22° C. As soon as the animals reached this body temperature, they were placed in a dimly illuminated heat reinforcement cage (Fig. 1) situated in a chamber maintained at $2.0 \pm 0.8°$ C. The body temperature of rats stayed constant at the desired level of 22° to 25° C in this 2° C environment, mainly because of prior shaving. However, it was necessary sometimes to elevate briefly the chamber temperature to avoid the drop of body temperature below 22° C. A T-shaped 8 g sensitive lever protruding 2.5 cm through the wall of the chamber was the only object in the cage besides the rat. Pressing of the lever closed a microswitch actuating the lighting of a 250 W infrared heating lamp for two seconds. The lamp was centrally placed 23 cm above the floor of the cage. Reactivation of the lamp was possible only after the lever was released and then pressed again. While the lamp was on, pressing of the lever had no effect. Each heat reinforcement delivered to the animals was recorded by a Varian Graphic Recorder.

The same recorder was used to monitor deep colonic temperatures by thermistors. The average body temperature from the beginning of the learning phase of each experiment until the moment the animals began to perform was integrated by use of a Planimeter for measuring curves and areas. Food and water were not available during the experiments.

FIG. 1. Heat reinforcement apparatus modified after Weiss and Laties

The procedure was developed so that: (a) Rats would be placed in a situation with strong motivation for learning. They would not survive if they failed to learn. (b) Rats would be exposed to accidental heat reinforcements giving the opportunity to learn. Moreover, these accidental heat reinforcements helped maintain the body temperatures of the animals at a level of 22° to 25° C during a 3-hr period, thereby providing ample learning time.

The criterion that the animals had learned to use heat reinforcement was a twofold one: (A) a marked increase in the rate of accidental reinforcements and (B) consistent use of the heat reinforcement lever. All judgments were confirmed by visual observations through a small window of the cold chamber.

Control Group

Seven male adult rats, each of them having a body weight matching that of an experimental rat, and in four cases taken from the same litters, were cooled the same way and to the same body temperatures as the experimental animals.

Before this cooling the animals did not have any hypothermia experience. After being rewarmed to a body temperature of 22.0° C, they were placed in the same experimental situation as the rats in the first group. Average colonic temperature, colonic temperature at the moment when animals began to perform, number of accidental heat reinforcements and time until the beginning of performance were measured using the same procedures as in the hypothermia-adapted group.

RESULTS

Hypothermia-adapted Group

The body temperature of the rats placed in the experimental chamber was maintained between 22° C and 25° C. Accidental heat reinforcements averaged 0.8/min. After an average of 58 (23–104) accidental reinforcements and after spending an average of 74 (34–116) min in the experimental chambers, all 7 rats suddenly began to use the reinforcement lever much more often, an average of 5.2 (4.6–6.0) times per minute instead of 0.8. The visual observations indicated increased interest in the lever too. Therefore, it was then concluded that the animals had learned to use the heat reinforcement apparatus. At this moment the body temperatures of the rats averaged 24.2° C (22.2° to 24.9° C). The mean body temperature of rats during the period of learning was 23.3° C (Table 1). After the rats began to perform, their body temperature rose steadily one degree for every 17 reinforcements (one degree every 3.3 min) until euthermia was reached. The average peak temperature was 37.0° C (36.5°–37.9° C). After reaching it, the reinforcement rate decreased by one-third.

Control Group

The body temperature of rats in this group was kept as close as possible to the body temperatures of rats in the hypothermia-adapted group. The average body temperature was maintained between 22.3° and 24.7° C. Nevertheless, 5 out of 7 rats failed to learn even though, being left in the chambers for the full 3-hr experimental period, they were exposed to more accidental heat reinforcements than the hypothermia-adapted rats. Two control rats which learned to perform for heat reinforcement began to perform later than any of the hypothermia-adapted rats (Table 1).

Table 1. Number of Prior Accidental Heat Reinforcements and Time in Experimental Chamber Body Temperature

Hypothermia-adapted rats					
Animal number	Body weight	Colonic temp., °C		Performance latency	
		Av. before performance	At moment of performance	Minutes	Accidental reinforcements
131	150	22.9	24.5	34	53
121	151	24.2	24.8	40	26
124	173	22.6	24.4	84	23
117	192	22.8	24.3	116	96
141	215	23.5	24.6	78	104
125	236	23.8	24.9	104	60
115A	261	23.6	22.2	64	47
Range	150-261	22.6-24.2	22.2-24.9	34-116	23-104
Average	197	23.3	24.2	74	58

DISCUSSION

Although hypothermia has been studied extensively for many years, only recent experiments revealed that an adaptation to a low body temperature is possible, e.g. it was shown that while rats survive 5-hr exposure to a body temperature of 15° C, they were able to survive a full 8 hr if cooled to 15° C four times prior to experiment (Popovic, 1959).

In our experiments learning and performance during hypothermia were shown to be much improved after animals were exposed twelve times to body cooling prior to the experiment. The hypothermia adapted rats performed at a lower body temperature and sooner than the controls. While all of the hypothermia-adapted rats performed, 70 per cent of the non-adapted rats kept at the same low body temperature failed to perform. This is in agreement with findings on 250–300 g rats which consistently failed to perform below 25° C (Panuska and Popovic, 1963). The two non-adapted rats which learned to perform did so after longer exposure than any of the hypothermia-adapted rats.

The improved performance of the hypothermia-adapted rats probably reflects the "better condition" of the central nervous system in the intact animal. Here we have a measurable parameter of a complex and coordinated nervous activity *when Performance for Heat Reinforcement begins in Hypothermia-adapted Rats maintained at a of 22° to 25° C*

Non-adapted rats					
Animal number	Body weight	Colonic temp., °C		Totals at moment of performance or at end of a 3-hr experiment	
		Av. before performance or during 3-hr experiment	At moment of performance	Minutes	Accidental reinforcements
144	150	22.3	24.5	132	109
146	153	22.9	no performance	(180)	132
145	176	24.7	no performance	(180)	181
149	188	22.3	no performance	(180)	65
147	202	22.7	23.8	175	178
98	245	23.0	no performance	(180)	76
94	253	24.0	no performance	(180)	61
Range	150–253	22.3–24.7	23.8–24.5	132–175	61–178
Average	195	23.1	24.2	154	114

which would be more difficult to measure and interpret in anesthetized animals or isolated tissues. How much the behavior is changed becomes evident when it is considered that adapted rats learn and perform at body temperatures barely above those at which locomotion stops and a physical anesthesia by cold is induced.

In interpreting our results, motivation must be considered too. We believe, however, that in our experiments this factor has been kept constant as much as possible. Age and body size are other factors which remain to be studied as factors in performance at a low body temperature. In the present experiments these factors were matched in each group of two animals in order to present easily interpretable results.

In summary: These studies have shown a new type of adaptation – adaptation to hypothermia – which is measurable in terms of operant behavior at a low body temperature. It was demonstrated further that after several exposures to hypothermia mammals can learn and can perform a simple technique even at a low body temperature of 22°–25° C, which is the lowest body temperature at which such a phenomenon was ever recorded.

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LONG-TERM VARIATIONS IN d.c. EYE-POTENTIALS

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THE corneo-fundal potential i.e. steady potential difference across the eye, which was discovered in 1849 by DuBois-Reymond through direct electrode-application on cat-eyes, is now measured in humans during long-term adaptation tests, through wide-range, high-impedance, fast response multi-channel d.c. amplifier-recorder systems by continuous registration of potential differences between pairs of non-polarizable (silver–silver chloride) surface electrodes placed equidistantly from the corneas in the horizontal (and vertical) planes about the ocular orbit. A periodic pattern of eye-potential variation due to light, and to dark adaptation, has been found to be superimposed on a diurnal base-line fluctuation of longer period in the standing ocular potential. Results integrating longterm adaptive changes in eye potential level, to changes in eye motion rate, and accuracy of oculomotor performance, are presented in detail, and related to variations in metabolic state (body temperature) and rate changes on repetitive perceptual and tapping tasks, and to oxygen consumption.

SUMMARY REPORT

H. HENSEL

In his opening remarks Hensel stated that physiological adaptation is part of the fundamental ability of the organism to maintain homeostasis. After deviation of physiological factors because of the influence of stressors these factors return to the initial value; in the course of the time, they normalize.

Physiological adaptation can be classified by its time course as follows:

(1) Acute regulations within time intervals ranging from seconds to hours.
(2) Slower responses of organisms to environmental changes ranging from hours to months. They are included in the terms acclimation, acclimatization and habituation.
(3) Adaptation in the evolutionary sense.

Homeostasis is maintained by feed-back controls in which the central nervous mechanisms play an essential part. Such central nervous mechanisms can change by the influence of a chronically repeated stressor (Glaser). As Hensel and Glaser state, the stressor can influence the central nervous system directly, or more often may reach the central nervous system by the inflow from receptors.

There are other cerebral mechanisms of adaptation: Conditioning and learning. Conditioning means that an existing response can be produced by a new stimulus, and learning means that a new response has been acquired or an existing one modified (Glaser). A major part of adaptation to new environments is probably a diminution of the responses to environmental stimuli, brought about by habituation; there is evidence that this complex coordination takes place within the cerebral cortex.

A review about the time factor in adaptation given by Hildebrandt deals with the duration of stimulation, the exposure time, synchronization of rhythmic changes during adaptation, the time course of adaptation and the relation of biological time phases and adaptation.

Significant adaptive changes need different time during exposure to different stressors. A single water, salt or glucose stress produced strong adaptive effects whereas hypoxia or cold did not cause any changes until after two or three exposures. Intermittent stimuli and exposure to stressors are more stressful than continuous exposure.

Differences of natural and experimental adaptation possibly depend on the daily temperature rhythm, which is not taken into account in experimental adaptation. Therefore the problems of synchronization can be studied best in natural conditions.

Light and temperature play a dominant part as synchronizers. This is demonstrated in several examples. Adaptation by means of synchronization is one of the later economical forms of adaptation.

Hensel reported about experiments and stated that the course of adaptation to heat was the same if people were exposed to heat in the morning or in the afternoon. It was not clear whether the degree of the adaptation did vary, depending on whether the stimulus was applied in the morning or in the afternoon.

A number of adaptate sequences are known in cold adaptation, altitude adaptation and strength-training. The course of adaptation is independent of the development kinetics of the adaptates.

The time course of adaptation possibly is dependent on the time concentration of the stimulus (Schaefer). With different strengths of the stimulus different regulatory systems are called into play. These various regulation mechanisms mainly influence the time course in functional compensations (Hildebrandt).

Normalization during adaptation often has a periodic course and is interrupted by acclimation crises. This is demonstrated by examples of balneo-therapeutic treatment or intermittent hypoxia.

Finally Hildebrandt demonstrated that age of the individual has a strong influence on adaptive abilities and that adaptation is influenced by long-term biological rhythms.

Blatteis, Wilson and Tromp discussed the possible integration of different stressors and the influence of more than one stressor on the reaction of the organism. The consideration of the time course of adaptation to different stressors seemed to be a difficulty in approaching the problem of adaptation.

Betz reported about similarities and differences during chronic exposure to noise, hypoxia and CO_2-excess on the cerebral circulation in cats. By thermoelectric measurements he recorded local cerebral blood flow continuously in free moving conscious cats for several months.

In all three types of stressors the initial deviation returned to normal values if the stimuli were not too strong.

The trend of the curves was not constant but showed periodic changes. The time course of adaptation was dependent on the intensity and the duration of the stressors and on the intervals between the stimuli. The same system needed different times for adaptation to the different stressors and this time was independent of the amplitude of the initial deviation.

Adaptation of cerebral blood flow to CO_2 seems to be a pH dependent effect (Schaefer). The diurnal rhythm (Tromp) influenced especially the adaptation to emotional stress.

The development of non-shivering heat production in the course of adaptation to cold was compared with the thermogenesis of newborn animals. Brück demonstrated electromyographic and metabolic studies in unanesthetized newborn guinea-pigs and kittens. Electrical activity of the musculature remained at zero level in cold environment although oxygen consumption rose by 200–300 per cent over the basal rate. From the second week of life onwards, shivering heat production developed. Within the first days of life oxygen consumption could be markedly reduced by Hexamethonium bromide whereas later on the effect of that drug was much less effective. It is suggested that the development of non-shivering heat production in the course of cold adaptation might be thought of as a re-manifestation of the normal heat production mechanism.

Blatteis confirmed the findings of Brück concerning shivering and oxygen consumption in his experiments in the newborn rabbit.

There are differences in the contents of adrenalin and noradrenalin in the medulla of newborn and adult animals and a different activity of the thyroid (Gale). One may assume that these differences contribute to the non-shivering thermogenesis (Brück). Body movements of the newborn do not play an essential role in the non-shivering thermogenesis.

Studies of Popovic, Panuska and Popovic have shown a new type of adaptation – adaptation to hypothermia – which was measured in terms of operant behavior at a low body temperature. It was demonstrated further, that after several exposures to hypothermia rats can learn and can perform a simple technique even at a body temperature of 22°–25° C.

Finally Kris reported about long-term variations in d.c. eye-potentials. A periodic pattern of eye-potential variation due to light, and to dark adaptation, has been found to be superimposed on a diurnal base-line fluctuation of longer period in the standing ocular potential.

ADAPTATION TO ARTIFICIAL ATMOSPHERES INCLUDING HIGH PRESSURE ENVIRONMENT

Chairman: K. E. Schaefer

EFFECT OF EXPOSURE TO INCREASED CO_2 LEVELS ON ALVEOLAR MITOCHONDRIA AND LUNG SURFACE TENSIONS

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Abstract — Exposure to a 15 per cent CO_2 atmosphere caused in the lungs of guinea pigs aside from typical hyaline membranes, degenerative alterations in the lamellar bodies of the granular pneumocytes. The latter changes paralleled the fluctuation in pulmonary surface tension, a fact pointing to the lamellar bodies as the site of origin of the pulmonary surface active agent.

Zusammenfassung — 15% CO_2 in der Atemluft verursacht in den Lungen von Meerschweinchen ausser hyalinen Membranen degenerative Veränderungen der Lamellarkörperchen (pathologische lamellenförmige Transformation der Mitochondrien) der granulären Pneumozyten (grosse Alveolarepithelzellen). Die Veränderungen der Lamellarkörperchen verliefen parallel zu den Schwankungen der Oberflächenspannung dieser Lungen, ein Ergebnis, das auf die Lamellarkörperchen als Ursprungsort des die Oberflächenspannung beeinflussenden Materials hinweist.

Résumé — L'exposition à une atmosphère contenant 15% de dioxyde de carbone cause dans les poumons de cobayes des dégénérescences de l'épithélium alvéolaire en plus des membranes hyalines qui s'y forment généralement. La modification de l'épithélium alvéolaire va de paire avec les variations de la tension superficielle des poumons. Cette constatation indique que cet épithélium est à l'origine de la matière régissant la dite tension superficielle.

THE concentration of surface active agent in lungs affected by hyaline membrane disease (respiratory distress in the newborn) is known to be considerably decreased (Avery, 1962). Increased concentrations of CO_2 in the atmosphere will produce alveolar and bronchiolar hyaline membranes (Niemoeller and Schaefer, 1962). Re-examination of the latter phenomenon was carried out on guinea pigs which were exposed for periods of 1 hr to 14 days to an atmosphere containing 15 per cent CO_2 (Schaefer, Avery and Bensch, 1963). Animals were sacrificed after 1 hr, 6 hr, 1, 2, 4, 7, and 14 days of exposure and the lungs examined with the light and electron microscope as well as for their concentrations of surface active agent. The latter studies were carried out on lung extracts with the surface tension measured with a modified Wilhelmy balance. The tissues for light and electronmicroscopy were fixed with glutaraldehyde (Sabatini, Bensch and Barrnett, 1963).

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Electronmicroscopic studies of the lung revealed the usual three types of alveolar cells: the phagocytic pneumocyte or alveolar macrophage; the membranous pneumocyte or alveolar lining cell and the second type of alveolar lining cell, the granular pneumocyte. The latter is known by several names such as large alveolar lining cell, niche cell, etc. The granular pneumocyte contains numerous electron-opaque structures which measure up to 3 μ in length. These are usually called lamellar bodies or lamellar transformations because of the characteristic lamellar arrangement of their electronopaque bars enclosed in a vesicle and because they consist of enlarged transformed mitochondria which have accumulated large quantities of lipoprotein.

We observed in control animals the previously suggested release of lamellar bodies into the alveolar space. This finding supports the assumption that the surface active substance of the lung originates in these transformed mitochondria (Klaus *et al.*, 1962). Further evidence for this was provided by the changes produced in lamellar bodies by CO_2. Exposure for 1 day caused a complete absence of the electronopaque lipoproteinaceous material in these structures, a finding which coincided with the maximum in decrease of concentration of surface active agent as indicated in the maximal elevation of surface tension. A moderate increase in amount of this agent was observed on the next day, i.e. after 2 days of exposure to CO_2. Lamellar bodies exhibited at this time some distortion of their internal structures, yet by now definitely contained material of high electronopacity suggestive of lipid or phospholipid. At day 4 to 7 after the start of an exposure experiment one finds an almost normal pulmonary surface tension and granular pneumocyte of near normal structure.

The earliest changes produced by CO_2 (1-hr exposure) was the swelling of the cytoplasm of the membraneous pneumocyte. This caused an increase in the width of the air–blood barrier; it was accompanied by a decrease in the pinocytotic activity of these cells, but did not affect the endothelial cells lining the capillaries of the alveolar septa. Edema fluid appeared in the alveolar sacs after 6 hr of exposure to CO_2 and after 24 hr there was necrosis of numerous membranous pneumocytes, leaving behind naked basement membranes. The capillary transudate contained now, focally, strands of fibrin. The predominant feature, however, was inspissated edema fluid in form of typical hyaline membranes (in alveoli and respiratory bronchioli) which consisted of a moderately electronopaque coarsely granular matrix which may contain cell debris and fibrin. Although neutrophillic polymorphonuclear leucocytes were frequently observed within capillaries, often as early as 1 hr after onset of an experiment, they are rarely found outside a blood vessel. The described structural composition of the hyaline membranes is almost identical with that described by Campiche (1692) who studied these structures in lungs of human newborns that had succumbed to hyaline membrane disease. These membranes disappeared gradually from day 2 to 4 after the onset to continuous CO_2 exposure and the membranous pneumocytes returned to their normal appearance within this period of time.

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ADAPTATION TO HIGH PRESSURE ENVIRONMENT*

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Abstract – Results of animal and human experiments carried out at U. S. N. Medical Research Laboratory (NMRL) under increased pressures using helium – oxygen – nitrogen gas mixtures are reviewed. In one study three subjects lived under seven atmospheres (corresponding to 200 ft depth of water) for 12 days without encountering difficulties. Findings demonstrate the feasibility to safely station men at certain points on the submerged continental shelf.

Zusammenfassung – Es wird über die Ergebnisse von Experimenten an Tieren und Menschen berichtet, die im Naval Medical Research Laboratorium in New London mit Helium – Sauerstoff – Stickstoff – Gasmischungen ausgeführt wurden. In einem Experiment lebten 3 Versuchspersonen beschwerdefrei 12 Tage unter 7 Atmosphären Druck (70 m Wassertiefe). Diese Befunde zeigen, dass Menschen mit genügender Sicherheit für ihr Leben unter Wasser stationiert werden können.

Résumé – On rapporte ici les resultats d'essais effectués au laboratoire de recherches médicales de la marine des Etats-Unis, à New London, sur des animaux et des hommes exposés à de hautes pressions et respirant des mélanges gazeux (hélium, oxygène, nitrogène). Au cours d'un essais, 3 sujets ont vécu 12 jours sous une pression de 7 atmosphères (correspondant à 70 m de profondeur) sans éprouver de difficultés quelconques. Ces resultats démontrent la possibilité de placer, sans danger pour eux, des hommes imergés aux points principaux du socle continental.

ADAPTATION TO HIGH PRESSURE ENVIRONMENT

About six years ago, personnel of the Naval Medical Research Laboratory began to explore new approaches to the old problem of inner-space exploitation. The reasons for this interest are apparent, from civilian and military points of view alike. For military purposes, the capability of undetected underwater existence and construction might add a new and potent string to the bow. On the other hand, this research, if successful, would certainly enhance civilian scientific utilization of oceanic resources. At the time, it seemed a worthwhile goal; and it was pursued with enthusiasm.

At first, it appeared that two major problems were involved: the choice of respirable gas mixture at any depth; and the ultimate question of decompression.

* Portions of this paper were presented at a meeting of the American Academy of Occupational Medicine, and will appear in the Archives of Environmental Health.

Initially, it was necessary to provide a gas mixture which would minimize both narcosis and breathing resistance; next, the problem of decompression after total body saturation required resolution. Since the final operational application would involve exposure of man to gas pressures of up to twenty atmospheres for infinite periods of time, a great deal of basic experimental work required attention.

As a beginning, it was desirable to reconfirm the probability that compressed air would not be a satisfactory breathing medium for man under these conditions. Although this likelihood had been pointed out by the work of Drinker and his associates some three decades past, the earlier experiments were repeated, with some extensions. Shortly, it could be demonstrated that compressed air, breathed at an equivalent sea depth of 200 ft, was lethal for selected Wistar strain rat populations after 35 hr of continuous exposure. Examining the hypothesis that the increased partial pressure of oxygen caused death in this instance, equivalent groups of animals were exposed to an atmosphere in which the partial pressure of oxygen was held at 160 mm/Hg, with nitrogen gas making up the pressure differential to seven atmospheres. In this experiment, all but one of 16 animals survived a 14-day exposure, but specific and irreversible lung lesions were found in the case of all survivors. These lesions were generally attributed to the density of the breathing mixture, although consideration was given to the narcotic effect of nitrogen at this depth, insofar as it might alter normal respiratory patterns.

A final check was made on the lethal effect of elevated oxygen partial pressures. Another matching rat group was exposed, under similar conditions of temperature and humidity, to an atmosphere of 100 per cent O_2, at a pressure of approximately 22 psi absolute. This exposure yielded an oxygen partial pressure of about 1120 mm/Hg, equal to that of the initial experiment at 200 ft (103 psi absolute), which had previously resulted in a 100 per cent mortality after 35 hr. In this experiment, with reduced gas density and with the element of nitrogen narcosis excluded from the design, 100 per cent mortality was again reached after 35 hr of exposure. Data from these experiments evidenced the predictable lethality of oxygen, with respect to animal subjects.

Considering that the specific deadly effect of high PO_2 had been demonstrated, and could be controlled, the next effort was to reduce the density of the inert gas component. If nitrogen proved too heavy, the obvious lighter inert gas of utility was helium.

In the U. S. Navy, helium and oxygen mixtures had been used for divers' breathing sources for some decades, covering thousands of hours of intermittent human exposure. Nevertheless, many competent physiologists were convinced that atmospheric nitrogen was essential to mammalian existence. It was necessary to complete a number of experiments in which nitrogen was absent from the respirable atmosphere, to settle this point at an animal level. Following the neglected example of Barach, with sophistication of design parameters and a larger number of animal subjects, a sizable colony of rats was exposed to an atmosphere of 80 per cent He, 20 per cent O_2, for a period of 16 days, with no adverse physiological effects, immediate or delayed. Thus, a long series of helium – oxygen exposures was commenced.

At first, adhering to original design parameters, and with careful control of environment, rats were exposed to the extreme depth of 200 ft, utilizing an atmosphere of 3 per cent oxygen, 97 per cent He. All exposures were continuous for a 14-day period; and the protocol of extensive biochemical, physiological, and histopathological examination of all subject animals was maintained rigidly. Subsequently, animal experiments were extended under high pressure to encompass four more species, including goats and squirrel monkeys. After two additional years of successful experimentation, it could be reported that all animals exposed to a selected mixture of helium, oxygen, and lesser quantities of inert gases not only survived a 14-day exposure at a simulated depth of 200 ft, but could be safely returned to sea level with no physiological damage (Workman, Bond and Mazzone, 1962). Decompression problems, and treatment of decompression accidents involved in such an exposure, were clarified in a separate series of experiments. After more than four years, the animal exposures were concluded.

In 1962, the Secretary of the Navy granted permission for utilization of human subjects in extension of this project. Shortly thereafter, following a cautious plan, the first set of volunteers was exposed to an essentially nitrogen-free atmosphere, for a total exposure of 144 hr. In this significant experiment, the average composition of the ambient atmosphere was 21.6 per cent O_2, 4.0 per cent N_2, 74.4 per cent He. Three human volunteers were selected for the exposure. Choice was determined by age, environmental chamber experience, and available physiological information. As in the case of our animal experiments, all parameters of blood chemistries and morphologies were carefully evaluated; in addition, EKG, EEG, metabolic values, and a multitude of psychophysiologic test values were obtained.

In this experiment, all major goals were achieved, and the human subjects completed the exposure with no measurable physiological decrement. Incomplete analysis of the test results, however, indicate a clear-cut stress response, a potential bacteriological problem, and a formidable problem of body temperature control. In addition, there was a persuasive suggestion that the inert gases of man's respirable atmosphere may exert a specific physiologic effect on the exposed individual.

Intriguing evidence indicated that the sum total of the effects of a synthetic atmosphere might be advantageous to the human organism. In short, based on early findings, it seemed possible that fresh, sea level air might not necessarily be the best of all possible atmospheres for human existence.

From data yielded by this experiment, it was possible to proceed to the next phase, requiring human exposure at 100 ft of simulated sea-water depth for a period in excess of 6 days. This experiment, accomplished in the chamber complexes at the Navy Experimental Diving Unit, involved use of a respirable atmosphere of 7 per cent O_2, 86 per cent He, and 7 per cent N_2. As in the previous phase, a wide range of physiological and psychological values were recorded daily for all subjects.

In addition, because of the unusual configuration of the pressure complex, the subjects were able to perform several hours of underwater work at this pressure daily, to simulate conditions of open sea habitation. Critical evaluation of the data from this exposure, when completed, indicated that although no physiological decrement was apparent in the course of the experiment, there were definite problems with respect to body temperature control and vocal communications. The accelerated thermal conductive properties of helium required maintenance of an ambient temperature of 88° F, for subjective comfort; and the unique physical properties of the gas combine to distort the human voice, under pressure, beyond ordinary recognition.

Attuned to these problem areas, a final human laboratory exposure was made in August 1963. Again, three Navy volunteers were utilized; two of whom were veterans of previous experiments. In this exposure, accomplished at the Naval Medical Research Laboratory, the subjects were compressed to an equivalent seawater depth of 200 ft, for a period of approximately 300 hr, with subsequent decompression amounting to 28 hr. The gas provided for this exposure was approximately: 3.5 per cent O_2; 4.5 per cent N_2; 92 per cent He.

In this final experiment, both physiological and psychological test parameters were expanded and sophisticated. In all, approximately 100 items of psychophysiological data were acquired daily from each subject. Repetitive and cumulative material failures complicated the operation, and provided a very realistic stress situation with respect to experimenters and subjects alike; nevertheless, the entire run was successfully accomplished, without decompression sequellae. All biochemical, hematological, and other physiological values of subjects remained within normal limits, with the exception of the conventional stress indicators, which reflected clearly initial exposure to the hazardous experimental situation, and to subsequent potentially fatal material casualties.

The persistent problems of thermal protection and voice communication, however, were definitely intensified in the course of this exposure. In order to maintain a "shirt-sleeve" environment, at 80 per cent R.H., an ambient temperature of 91° F was required. Communication, even among the subjects in the chamber, was quite difficult; with outside observers, it was nearly impossible. Bacteriologic studies of fecal and oral samples failed to reveal development of any pathogenic strains, and no significant shifts of bacterial balance were found in any of the subjects during the 12-day exposure. Metabolic studies showed no evidence of alteration in the respiratory quotients of the subjects as a group, and caloric intake was equivalent to that obtained in the baseline studies.

Pulmonary function studies produced evidence of adaptation to the high pressure environment. Vital capacity showed a 20 per cent decrease after 4 hr associated with a fall in expiratory reserve volume. However, by the fifth day of exposure both parameters had returned to control values. Since the density of the ambient gas was 1.5 times the density of air, one would expect an increase in airflow resistance which was indicated in:

(1) a fall in maximum breathing capacity from 129 per cent of the predicted value to 83 per cent, (2) a 13 per cent decrease in 1 sec timed vital capacity, and (3) a 33 per cent reduction in peak expiratory flow rate (Lord, Bond and Schaefer, 1964).

As a result of these animal and human studies, the stage has been set for operational application of the work. It would now appear that we can safely station men at any point on the submerged continental shelf, with a reasonable expectancy of useful performance for prolonged periods of time.

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ADAPTATION AUX HAUTES PRESSIONS

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Abstract – Strong evidence exists that the human organism can compensate for variations (in absolute pressure differentials in a ratio) from 1 to 2 : 1 in the atmosphere which he breathes. The authors have endeavored to apply these experiences to a series of practical tests in which man lived and performed work for prolonged periods in the undersea environment. Work efficiency in these conditions was far superior to that obtained by the usual techniques of diving (repetitively) from the surface. The first test off Marseille was conducted by two subjects living submerged for 7 days in compressed air at a depth of 10.5 m. They performed working dives from this base to depths of 25 m. A second test was conducted in the Red Sea (at Shaab Rumi) near Port Soudan with two teams submerged simultaneously: Five subjects lived at a depth of 9 m in compressed air (open circuit from surface) for one month and performed working dives from this base to depths of 70 m. Two subjects lived at a depth of 26 m for one week in a compressed mixture of air and helium and performed dives from this base to depths of 100 m.

The experiments have proved that humans can adapt successfully to the described conditions of life.

Zusammenfassung – Es sind genügend Beweise vorhanden, dass der menschliche Organismus Druckschwankungen von 1 bis 2 : 1 der Atmosphäre ertragen kann. Die Autoren haben diese Erfahrungen praktisch erprobt bei Männern, die längere Zeit unter Wasser lebten und dort Arbeiten ausführten. Die Arbeitsleistung unter diesen Bedingungen war weitaus grösser, als sie bei der üblichen Tauchtechnik von der Oberfläche aus erreicht wird. Im 1. Versuch lebten 2 Personen 7 Tage in der Tiefe von 10,5 m. Sie leisteten Arbeit beim Tauchen bis zu Tiefen von 25 m. Beim 2. Versuch im Roten Meer waren 2 Gruppen gleichzeitig beteiligt. Eine Gruppe von 5 Personen lebte 1 Monat lang in 9 m Tiefe (mit offener Verbindung an die Oberfläche). Die Personen tauchten bis 70 m Tiefe. Die andere Gruppe mit 2 Personen lebte eine Woche lang in 26 m Tiefe und tauchte bis 100 m Tiefe. Sie atmeten ein Gemisch von He mit Luft. In beiden Versuchen lebten die Beteiligten im Überdruck. Die Untersuchungen haben gezeigt, dass sich der Organismus erfolgreich an die beschriebenen Lebensbedingungen anpassen kann.

Résumé – De nombreux indices laissent à penser que l'organisme humain peut compenser des variations de pression de 1 à 2 : 1 dans l'atmosphère qu'il respire. Nous avons essayé d'appliquer ces présomptions à une série d'essais pratiques durant lesquels l'homme vit et travaille pendant de longues périodes dans une ambiance sous-marine. La qualité du travail fourni dans ces conditions particulières fut bien meilleure que celle obtenue d'ordinaire par des scaphandriers opérant depuis la surface. Le premier essai, effectué au large de Marseille a permis à deux individus de vivre durant 7 jours dans de l'air comprimé et cela par 10,5 m de fond. De cette base, ils ont effectué des travaux en plongée jusqu'à une profondeur de 25 m. Cette experience eut lieu sous une surveillance médicale très stricte. Un second essai eut lieu dernièrement dans la Mer Rouge à Shaab Rumi près de Port Sou-

dan où deux groupes furent immergés simultanément : Cinq individus vécurent durant un mois par 9 m de fond dans de l'air comprimé (circuit ouvert à partir de la surface), opérant de cette base des travaux jusqu'à une profondeur de 70 m. Deux individus vécurent par 26 m de fond durant une semaine dans un mélange d'oxygène et d'hélium, partant de là pour des plongées pouvant atteindre 100 m. Pourtant, on a prouvé par les essais qui ont déjà été effectués que l'homme peut parfaitement s'adapter aux conditions de vie décrites plus haut.

L'homme est adapté à des conditions de vie moyennes, mais cette adaptation même comporte une certaine marge et permet à son organisme de s'accommoder, même pour de longues durées, de conditions franchement différentes.

L'écart maximum tolérable est souvent difficile à chiffrer, les divers éléments réagissant les uns et les autres, et souvent l'industrie de l'homme, par exemple celle des vêtements, a une influence prépondérante dans l'acclimatation.

Cependant, en ce qui concerne la tolérance des variations de la pression atmosphèrique une règle assez simple semble se dégager.

Dans le sens d'une diminution d'abord, on trouve en plusieurs points du globe des populations qui se sont adaptées complétement à la vie à des altitudes de l'ordre de 5000 m, donc sous une pression moitié moindre. Les études faites sur les alpinistes et les aviateurs ont confirmé qu'au delà de ce rapport l'adaptation de l'organisme ne se faisait plus de façon satisfaisante.

Dans le sens de l'augmentation, il est difficile de se référer à des cas naturels, et les effets de celle que l'on rencontre parfois, par exemple dans des mines très profondes sont toujours masqués par ceux d'autres modifications simultanées et très importantes de température, d'humidité, etc.

Cependant, dans le cas de la plongée et des travaux sous pression en général nous avons un indice assez net en ce qui concerne le problème particulier de la décompression et là encore Haldane a mis en évidence un rapport limité voisin de 2 à 1 au-delà duquel l'organisme n'arrive plus à compenser de façon satisfaisante les changements qui lui sont imposés.

Il n'est bien entendu pas question d'établir une prétendue loi physiologique, mais de faire saisir la marche du raisonnement qui nous guide dans la série d'expériences « Précontinent ».

En dehors des motifs presque sentimentaux que je viens d'exposer, nous avions pour nous appuyer une quantité importante de résultats expérimentaux, tant sur l'homme que sur les animaux. Des résultats intéressants apparaissent déjà dans les travaux de Bert (1878) et Haldane (1908, 1909). Mais surtout des travaux récents sur les animaux effectués les uns par Workmann, Bond et Mazzone (1962), les autres au G. E. R. S. en 1949, puis plus récemment (non publiés) nous donnaient une grande sécurité pour les premiers pas. Elle nous paraissait telle qu'il n'y avait pas lieu de reprendre des expériences de laboratoire déjà concluantes. Nous voulions au contraire, profitant par ailleurs de notre expérience dans le domaine sous-marin, faire tout de suite des expériences complètes et réalistes, à un échelon pratique, pour étudier simultanément l'adaptation à la pression et aux autres conditions du milieu dont l'influence sur l'organisme humain pouvait être tout aussi importante.

Nous avons parfaitement conscience de ce que cette décision peut avoir d'apparemment anti-scientifique. Mais si elle ne tient pas compte du sacro-saint principe

FIG 1. Expérience précontinent no. 1. Vue extérieure de «DIOGENE». Le Dr. Fructus et le Professeur Chouteau font passer des tests psychotechniques aux deux Océanautes

de dissociation des facteurs elle répond en fait à la nécessité de synthèse qui réapparait tôt ou tard. Et surtout nous avions conscience que la voie était large ouverte, et qu'il importait surtout de ne pas perdre de temps à rechercher des précisions sans intérêt immédiat.

La première expérience. Précontinent I a eu lieu du 14 au 21 Septembre 1962 en rade de Marseille.

La base sous-marine appelée Diogène, était constituée par une chambre cylindrique à axe horizontal de 25 m^3 flottant entre deux eaux et ancrée sur le fond par plus de 30 tonnes de gueuses.

Elle comportait à la partie inférieure une ouverture de 1 m de diamètre par laquelle se faisait l'équilibre à une profondeur de 10,50 m. Une extrémité contenait un mobilier sommaire pour deux hommes et comportait un hublot de vision extérieure, l'autre servait de salle d'habillage «humide» et de réserve à matériel de plongée et de sécurité.

Un faisceau de fils et de tuyaux la reliaient à un poste central situé à 200 m de distance sur l'Ile de Pomègue, et d'où parvenaient : l'air comprimé (400 à 500 l/m), l'eau douce froide ou chaude, et l'électricité.

Les liaisons comportaient un interphone, un téléphone, un microphone et une caméra de télévision permettant la surveillance continue des sujets. Ceux-ci disposaient, en outre, d'un poste de télévision recevant les émissions de la R.T.F. La Chambre de Commerce de Marseille nous a prêté pour la réalisation de cette installation une aide inappréciable.

Des plongeurs assuraient les transports de nourriture et matériel en contenants étanches.

Les deux sujets, tous deux plongeurs professionnels entraînés, A. Falco et Wesly, ont été soumis tout au long de l'expérience à un contrôle médical extrêmement minutieux et comportant de nombreuses mesures et analyses. Il était assuré par le Docteur Fructus et le Professeur Chouteau, tant en surface avant et après l'expérience, que dans Diogène, ou même au cours des plongées quotidiennes des sujets.

En fait son importance et sa durée (jusqu'à 4 hr par jour) étaient telles qu'il faut sûrement en tenir compte parmi les causes susceptibles d'avoir agi sur les sujets pendant l'expérience.

Parmi les facteurs extérieurs importants notons que la température de l'eau, de 21° C au début de l'expérience, est tombée à 16° C par suite d'un coup de mistral du 3ème au 6ème jour. Les sujets travaillaient en moyenne 4 à 5 hr/jour en plongée entre 5 m et 25 m. Ils utilisaient des autonomes à grande capacité d'air comprimé, et portaient des vêtements humides en néoprène épais.

Un compte rendu médical de cette expérience a été donné par Fructus, et Chouteau (1963).

Nous ne pouvons en citer que des extraits très brefs:

ÉTUDES PHYSIOLOGIQUE DES DEUX SUJETS EN EXPÉRIENCE

Avant l'expérience les deux sujets ont été soumis à un certain nombre d'examens.

(1) Examen clinique, suivant le protocole adopté à notre consultation de médecine sportive, radiologie pulmonaire.

(2) Examen neuro-psychiatrique avec interrogatoire psychiatrique, EEG, examens psychologiques, tests.

(3) Exploration cardio-vasculaire: clinique, électrocardiographique, avec test de Master et test de Flack.

(4) Explorations biologiques, portant sur: l'azotémie, la glycémie, l'uricémie, les protides et les lipides sanguins, le cholestérol sanguin total et estérifié, le protéinogramme, le lipidogramme, l'hémogramme, la vitesse de sédimentation, le thromboélestogramme, ainsi que l'hématocrite et l'ionogramme sanguin.

Dans les urines, en plus de examens classiques de dépistage, on a dosé l'urée, l'acide urique, les chlorures, la créatimine, le sodium et le potassium.

On a mesuré aussi l'élimination des métabolites hormonaux: 17 cétostéroïdes, par la méthode de Zimmermann; 17 hydroxy 20 céto, par la méthode de Porter et Silber, et les corticoïdes réducteurs totaux, selon la technique de Jayle au bleu de tétrazolium; ainsi que les catécholamines totales.

On a dosé également l'excrétion d'uropepsine.

La plupart de ces examens cliniques, psychotechniques et biologiques, ont été renouvelés plusieurs fois (mais moins souvent que nous ne l'aurions souhaité), durant le séjour sous la mer et le deuxième jour après la sortie.

Nous avons réuni ainsi le plus possible d'éléments susceptibles de nous éclairer sur le comportement physiopathologique des deux sujets pendant une semaine de vie en atmosphère comprimée, sous la mer, et respirant un air dont la pression partielle d'oxygène était sensiblement le double de celle existant à la surface.

L'évolution de ces divers éléments fait l'objet d'un volumineux rapport que nous allons tâcher de résumer.

Parmi les signes cliniques, nous passerons rapidement sur le poids (léger amaigrissement) ; le pouls et la température, stables ; la tension artérielle qui a légèrement fléchi chez (W) ; les épreuves cardio-vasculaires qui sont demeurées remarquablement normales.

Le comportement, que nous avons suivi de très près (nous étions, en moyenne, 4 hr par jour auprès d'eux), mérite une certaine attention.

COMPORTEMENT DE FOND

Si certains incidents sont venus, au cours de l'expérience, modifier certains aspects du comportement des sujets, on n'en enregistre pas moins une certaine stabilité dans:

– leur volonté de poursuivre l'expérience;

– leur coopération aux examens médicaux;

coopération qui, comme chez tous les sujets sportifs, en bonne santé, est loin d'être parfaite. laisse toujours la porte ouverte à certaine négligence, s'accompagnant toujours d'une incompréhension de la rigueur qui doit présider aux prélèvements et aux examens (exemple: le refus de prendre la température autrement qu'axillaire a eu lieu dès les premières 24 hr), mais tout cela n'a été ni aggravé, ni amélioré par le séjour sous-marin;

– l'absence apparente de claustrophobie, et toujours apparemment du moins, l'attitude diamétralement opposée d'agoraphobie;

– parallèlement à cette agoraphobie, l'absence d'exhibitionnisme et des attitudes se tenant dans les limites du naturel, surtout chez (F), en présence d'une observation pourtant constante;

– l'absence d'occupations intellectuelles et le peu d'intérêt manifesté pour les émissions de radio et de télévision;

– bref, un certain détachement du milieu terrestre qu'ils avaient quitté, et cela pour tous les deux, sans aucune crise, si brève soit-elle, de regret ou de nostalgie, seulement l'obsession — modérée sans doute et peu formulée, mais permanente, — de la période de transition lors du retour à la surface, avec les accidents possibles qu'elle pourrait comporter;

– pas de surexcitation particulière comme on aurait pu s'y attendre à cause de l'hyperoxie, sauf peut-être le matin du deuxième jour où, au moment du petit déjeuner, ils manifestaient une euphorie un peu excessive par rapport à leur comportement habituel;

– mais plutôt le contraire, une certaine nonchalance, un ralenti à peine sensible dans l'action, quelques manifestations, sinon de fatigue, du moins d'asthénie ou peut-être de paresse relative dont nous aurons à reparler, mais qui n'ont pas évolué au cours du déroulement de l'expérience.

– en revanche, pas du tout de ralentissement dans la nage sous l'eau, simplement, dans le travail sous l'eau, des efforts, pour eux habituels, leur ont paru un peu plus pénibles.

CRISES

Sur ce fond de stabilité se détachent des crises.

Les crises (si l'on peut employer ce terme pour des réactions, somme toute modérées, dans le comportement des deux bathynautes) se sont manifestées de façon suivante:

— Pour (*F*), un cauchemar à teinte fortement anxieuse au cours de la première nuit;

— Pour (*W*), rien de nettement apparent, mais, le soir du 2e jour, les deux sujets ont trouvé la plongée nocturne fatigante bien qu'elle n'ait duré que 55 min, ce qui est peu au regard de leur entraînement et du programme établi (5hr/jour, alors qu'ils n'ont plongé que 4 hr ce jour-là).

Le 3e jour, ils ont trouvé fatigant le maniement des gueuses sous l'eau et ont demandé à être dispensés de plongée de nuit. Cette attitude contraste avec celle du 4e jour où, malgré leurs troubles digestifs et les crises gastriques de (F), ils ont exécuté leur programme assez allégrement (4 hr 50 min de plongée).

Le 5e jour, ils n'ont travaillé sous l'eau que 3 hr 30 min mais sans se plaindre.

Le 6e jour: 4 hr 50 min; le 7e jour: 4 hr 5 min, mais avec beaucoup plus d'entrain et les plongeurs qui les accompagnaient ont pu admirer l'aisance et la vitesse de leurs évolutions sous l'eau.

La crise de fatigue, ressentie par (F) le matin de la sortie, a naturellement modifié son comportement pendant les dernières heures, mais cette crise avait certainement une composante psychique: inquiétude pour l'un de nous (Pr. Chouteau) qui s'était soumis à un délicat exercice d'évacuation en caisson monoplace, et peut-être, crainte inavouée d'accidents imprévisibles lors de leur retour à la surface.

Quoi qu'il en soit et globalement, le comportement des deux bathynautes s'est plutôt amélioré, stabilisé lors des derniers jours de leur séjour sous la mer.

Nous ne dirons que quelques mots des réactions psychomotrices qui ont été tout particulièrement scrutées à l'aide de nombreux tests (échelle d'intelligence de Wechsler-Bellevue, figure complexe et ordination de chiffres de Rey, test de rétention visuelle de Benton, ainsi que des tests de performance et la mesure des temps de réaction).

Ne pouvant entrer dans le détail, nous citerons simplement la conclusion de la psychologue:

«Nous n'avons pas mis en évidence, au cours de l'expérience, de troubles intellectuels ou psychiques, susceptibles d'entraver en quoi que ce soit l'adaptation des sujets.»

«Les fluctuations de l'efficience ont été légères et pas toujours concordantes. L'effet d'apprentissage, signe d'adaptation, s'est manifesté de façon évidente.»

Nous nous excusons de ne pas donner ici le détail des résultats des analyses effectuées, qui figurent dans la publication citée.

Citons les conclusions qui les résument:

Ce qui donne toute sa valeur à l'épreuve, c'est le remarquable parallélisme du comportement des deux sujets, surtout en ce qui concerne les réactions biologiques. Plus vives chez (W), plus amorties chez (F), mais comparables.

Chronologiquement, nous distinguerons trois phases:

1re phase, très précoce, avec crise d'adaptation caractérisée par:

- de l'angoisse, très contrôlée par (F) (sauf dans le sommeil) surcompensée par (W) (ce qui en aggrave les effets);
- une asthénie modérée, à tout prendre et peut-être euphorique;
- un ensemble de réactions métaboliques et hormonales, pouvant être pour la plupart apparentées au Syndrome d'Alarme, avec:

- chute de la glycémie;
- légère baisse des 17-CS;
- baisse plus marquée des 17-OHCS;
- fuite du potassium globulaire;
- élimination excessive du sodium (ainsi que du potassium, ce qui est moins explicable).

Tout cela transitoire, trop tôt apparu et trop vite corrigé pour être la conséquence d'une agression par l'action chimique d'O_2 ou de N_2 sous une Pp double de la normale. Il est difficile d'interpréter cette crise autrement que comme un stress psycho-neurogène.

2e phase. Du 2e au 4e jour, l'adaptation s'affirme, la vie parait décidément possible, l'activité redevient sensiblement normale. Mais une crise gastro-intestinale se développe, avec forte uropepsinurie, témoignage d'une deuxième crise d'adaptation, plus particulière, celle de l'alimentation, à ce genre d'existence.

Ou, peut-être, simple remous neuro-végétatif à prédominance vagale, consécutif au premier stress. Il est difficile de se prononcer à coup sûr.

3e phase. Les trois derniers jours, tout se passe comme si, détachés de la surface, les bathynautes avaient trouvé leur régime de croisière. Ils envisageraient favorablement un séjour beaucoup plus long. Plus rien n'altère leur dynamisme, sauf le souci de la remontée.

Toutefois, que ferait leur azotémie si l'expérience se prolongeait? Et cette anémie relative de compensation à une P O2 double de la normale ne risquerait-elle pas d'entrainer à la longue une sidération de l'hématopoièse?

L'irritation cutanée et ses petits foyers pyodermiques ne pourraient-ils pas évoluer vers une infection staphylococcique plus grave, faute d'air sec et de soleil?

Et que faut-il penser des très légers signes de souffrance corticale révélés par l'EEG?

Ces points d'interrogation, à vrai dire, ne sont pas suffisants pour nous priver d'optimisme.

Cette expérience avait donc montré que, conformément à nos prévisions, l'homme semblait capable de s'adapter à la vie sous une pression d'air double de la normale, et rester dans ces conditions capable de procéder à des travaux en plongée dont le rendement était considérablement accru en durée et en profondeur, la pression de référence pour la décompression étant bien celle de son nouveau milieu.

Cependant il subsistait deux points faibles:

- deux sujets seulement avaient été soumis à l'épreuve, tous deux plongeurs entrainés et tous deux d'une constitution exceptionnelle.
- la durée d'une semaine avait bien permis de constater que l'organisme des sujets, soumis à une agression, avait réagi et compensé d'une façon apparemment satisfaisante après 6 à 7 jours, mais la stabilité de cette compensation restait à prouver.

C'est pourquoi nous avons préparé l'opération Précontinent II, où, dans des conditions analogues de pression, d'atmosphère et de travail, un nombre plus élevé de sujets, aux caractéristiques moins homogènes, vivrait pendant un mois sans faire surface.

Pour des raisons topographiques la profondeur de référence n'a été que de 9 m au lieu de 10 prévus. Cinq hommes, Monsieur le Professeur R. Vaissière, Sous-directeur du Musée Océanographique de Monaco; A. Folco, dessinateur; P. Guilbert, cuisinier; C. Wesly et P. Vanoni, plongeurs; ont vécu durant un mois dans l'air comprimé à 1,9 atm, sans présenter de troubles particuliers pendant ni après leur séjour. Ils ont abondamment travaillé en plongée jusqu'à des profondeurs de 70 m.

De plus, la présence de ce relais sous-marin (prévu pour huit habitants) nous a permis d'effectuer dans les meilleures conditions de sécurité l'expérience, préliminaire de l'échelon suivant:

Dans une deuxième «maison», située à 26 m de profondeur, où une atmosphère synthétique d'air et d'hélium maintenait des conditions convenables, deux plongeurs, A. Portelatine et R. Kientzy ont vécu une semaine, effectuant des plongées jusqu'à plus de 100 m.

Eux non plus n'ont présenté aucun trouble inquiétant pendant ni après l'expérience.

Le dépouillement des résultats ainsi obtenus est encore en cours. De toute façon les contrôles médicaux par prélèvements et analyses n'ont pas été aussi détaillés que ceux qui avaient pu être pratiqués au voisinage immédiat de Marseille.

Les ressources des laboratoires de Port-Soudan étaient limitées, et le lieu de l'expérience en était à plusieurs heures de navigation. Mais les résultats de la surveillance clinique continuelle sont clairs et rien encore n'empêche de prévoir de nouveaux progrès.

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EFFETS DU SÉJOUR DANS UNE ATMOSPHÈRE À FAIBLE CONCENTRATION D'OXYDE DE CARBONE SUR LES RÉACTIONS CIRCULATOIRES ET RESPIRATOIRES A L'EFFORT MUSCULAIRE ET SUR L'ACUITE VISUELLE NOCTURNE

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Abstract – Experiments have been made on 12 subjects to study the influence of living in an atmosphere containing small concentrations of carbon monoxide, upon the cardiac and respiratory reactions to muscular work and upon night vision. With concentrations of 50 to 100 ppm of carbon monoxide in air, there was no respiratory reaction, but we observed an increase of cardiac acceleration during the effort and during consecutive rest. The effects upon night vision were small and inconstant. Smoking (source of CO) when being exposed to small CO concentrations (50 ppm) increases the cardiac acceleration during effort more than could be predicted from the corresponding CO concent of blood; furthermore, there is a significant rise of the morphoscopic minimum light level. It seems that there is a specific action of tobacco smoke distinct from the nicotinic effect.

Zusammenfassung – Es wurde die Wirkung des Aufenthaltes in einer CO-haltigen Atmosphäre auf die Herz- und Atmungsreaktion, die Dunkel-Sehfähigkeit und die Muskelaktivität untersucht. Bei Konzentrationen von 50 bis 100 ppm CO wurden keine Atmungsveränderungen gefunden. Man fand aber eine stärkere Herzbeschleunigung bei Arbeit und in der nachfolgenden Erholungphase. Die Dunkel-Sehfähigkeit wurde nur leicht und nicht dauernd beeinflusst. Rauchen als CO-Quelle während des Aufenthaltes in einer Atmosphäre mit 50 ppm CO steigert die Herzbeschleunigung mehr bei Arbeit als es bei der entsprechenden CO-Konzentration zu erwarten war. Eine deutliche Erhöhung der morphoskopischen Schwelle der Dunkel-Sehfähigkeit wurde festgestellt. Rauchen kann eine Wirkung haben, die unabhängig von den Konzentrationen des CO in der Atmosphäre ist.

Résumé – Des expériences portant sur 12 sujets ont été réalisées afin d'étudier les effets du séjour dans une atmosphère contenant de faibles concentrations en oxyde de carbone sur les réactions cardio-respiratoires, à l'exercice musculaire et sur l'acuité visuelle nocturne. Pour des concentrations en oxyde de carbone de 50 à 100 ppm il n'y a pas de réactions respiratoires mais une augmentation de la cardio-accélération au cours de l'effort et de la récupération. Les effets sur l'acuité visuelle nocturne sont faibles et inconstants. La consommation de tabac (source de CO) lors de l'exposition à de faibles concentrations de CO (50 ppm) augmente la cardioaccélération à l'effort de façon plus importante que ne le ferait prévoir l'oxycarbonémie correspondante; de plus, on observe une nette augmentation de seuil morphoscopique visuel nocturne. Il y aurait une action propre au tabac mais indépendante de l'oxycarbonémie.

La vie dans l'atmosphère artificielle d'un sous-marin, particulièrement d'un sous-marin nucléaire capable de rester isolé plusieurs mois de notre milieu naturel, pose une série de problèmes de nature diverse aussi bien physio-toxicologiques que psychologiques. Parmi ces derniers, le maintien d'un équilibre psychique satisfaisant au cours d'une croisière sous-marine monotone est un des plus ardus et aucun des moyens propres à le résoudre ne doit être négligé.

C'est ainsi que nous avons été amenés à nous demander si l'usage du tabac — actuellement proscrit à bord des unités françaises — ne devait pas être autorisé à l'avenir parce qu'il procure à certains sujets, on le sait, une détente psychologique certaine.

Mais, la fumée de cigarettes est, en milieu clos, un facteur de pollution atmosphérique très important; plusieurs centaines de substances dont un bon nombre est toxique ont été détectées aussi bien dans la phase particulaire (aérosol) que dans la phase gazeuse; dans cette dernière l'oxyde de carbone représente l'élément le plus dangereux par sa relative abondance et sa toxicité.

Une étude préliminaire sérieuse était donc nécessaire. Dans un premier temps nous avons évalué la quantité de tabac pouvant être fumée par un équipage et mesuré la quantité d'oxyde de carbone émise par les cigarettes utilisées. Dans un second temps, et c'est le résultat de ces recherches que nous rapportons ici, nous avons tenté de déterminer la concentration maximale en oxyde de carbone acceptable à bord d'un sous-marin pour que les chimistes et les ingénieurs puissent calculer la puissance des dispositifs d'épuration oxycatalytique à prévoir.

On sait que dans l'industrie la concentration maximale admissible est fixée à 50 parties par million; cette valeur ne pouvait — *a priori* — être appliquée telle quelle à l'atmosphère d'un sous-marin, d'une part parce que les sous-mariniers séjournent dans l'atmosphère polluée 24 hr sur 24 et n'ont pas la possibilité, comme les ouvriers, de se désintoxiquer en atmosphère normale, d'autre part parce que des membres de l'équipage ont à effectuer dans certaines circonstances des tâches physiques ou psychosensorielles épuisantes exigeant l'intégrité de leurs capacités.

Comme les travaux rapportés dans la littérature concernent généralement des valeurs d'oxycarbonémie assez fortes, il a paru nécessaire d'expérimenter sur des concentrations faibles de 50 à 100 ppm et d'en rechercher les effets sur des fonctions que l'on peut considérer comme devant être affectées en priorité puisqu'elles le sont très précocément par l'hypoxémie d'altitude: les réactions cardio-respiratoires à un effort musculaire intense et l'acuité visuelle nocturne (seuil morphoscopique élémentaire).

PROTOCOLE EXPÉRIMENTAL

Trois expériences dont nous rapellerons brièvement le but et le protocole général ont été faites dans la chambre climatique du Laboratoire.

Une expérience préliminaire de 24 hr a permis de déterminer les valeurs de carboxyhémoglobine correspondant à 50 ppm et de mettre au point les diverses techniques de mesure.

Dans la deuxième expérience d'une durée de dix jours les sujets ont été soumis à trois types de conditions expérimentales, chacun d'une durée de deux jours.

Phase 1: période initiale de contrôle, pas de CO, pas de cigarettes.

Phase 2: concentration de CO de 50 ppm, pas de cigarettes.

Phase 3: concentration de CO de 50 ppm, autorisation de fumer.

Phase 4: période finale de contrôle, pas de CO, pas de cigarettes.

Dans la troisième expérience dont le protocole diffère peu de la seconde, on a simplement ajouté une cinquième phase avec 100 ppm de CO et interdiction de fumer pour déterminer si les résultats obtenus dans la phase 3 de la 2 nd expérience étaient dûs à l'oxycarbonémie supplémentaire observée en fumant ou à d'autres composants de la fumée de cigarette.

Conditions Expérimentales

Chaque expérience a porté sur six sujets, fumeurs, préalablement sélectionnés et s'est déroulée dans une chambre climatique étanche d'un volume de 60 m^3, où l'on peut vivre confortablement. La température était réglée à 21° et l'hygrométrie à 75 pour cent (température effective 20° C). La pression atmosphérique était celle du niveau de la mer.

Pour se rapprocher le plus possible des conditions existant à bord d'un sous-marin et pour que nos résultats y soient applicables sans discussion, pendant toutes les phases des expériences la concentration en CO_2 était automatiquement réglée à 1% et la concentration d'oxygène était maintenue entre 20 et 21%. Des expériences antérieures nous ont montré qu'à ces valeurs on n'observe aucun effet sur les paramètres des fonctions explorées.

La concentration en oxyde de carbone était analysée en permanence (appareil doseur à infra rouge) et réglée automatiquement aux valeurs désirées à ± 4 ppm par admission contrôlée dans le circuit de ventilation d'un mélange tiré de CO et d'air comprimé.

Méthodes de Mesure Utilisées

Mesure du pourcentage de carboxyhémoglobine. Les mesures devant être faites une à deux fois par jour, la détermination de l'oxycarbonémie à partir du sang aurait exigé des prises de sang trop fréquentes et nous avons préféré recourir à la méthode dite «alvéolaire» qui mesure la concentration d'oxyde de carbone et d'oxygène à la fin d'un «rebreathing» de six minutes dans un sac rempli d'oxygène selon une technique inspirée de celle de T. Sjostrand (1948) et que nous pratiquons depuis de nombreuses années (Guillerm, 1959). Les résultats exprimés en carboxyhémoglobine sont précis à $\pm 10\%$ de la mesure.

Mesure de réactions cardio-respiratoires à l'effort. L'exercice musculaire consistait en une marche à 7 km/hr pedant 5 min sur tapis roulant avec pente de 10% (environ 1300 kg/min).

Avant l'épreuve, pendant celle-ci et lors des dix premières minutes de la récupération, la fréquence cardiaque était mesurée toutes les 30 seconde. Le débit respiratoire, la consommation d'oxygène et la fréquence respiratoire ont été également mesurés.

Mesure de l'acuité visuelle nocturne. Elle a été mesurée à l'aide d'un scotoptomètre de Beyne qui permet de déterminer le seuil morphoscopique élémentaire (S.M.E.). Cette mesure était pratiquée chaque jour à heure fixe; auparavant, les sujets avaient subi une préadaptation à 1500 milliamberts pendant 3 min suivie d'une adaptation de 30 min dans l'obscurité complète.

RESULTATS

Étude des Valeurs d'Hb CO *Mesurées*

On sait qu'à la fin de la journée, un fumeur présente un pourcentage d'Hb CO qui peut atteindre 10 pour cent et qui dépend du nombre de cigarettes consommées et de la façon dont il fume. Comme on peut le voir sur la figure 1, nos sujets étaient

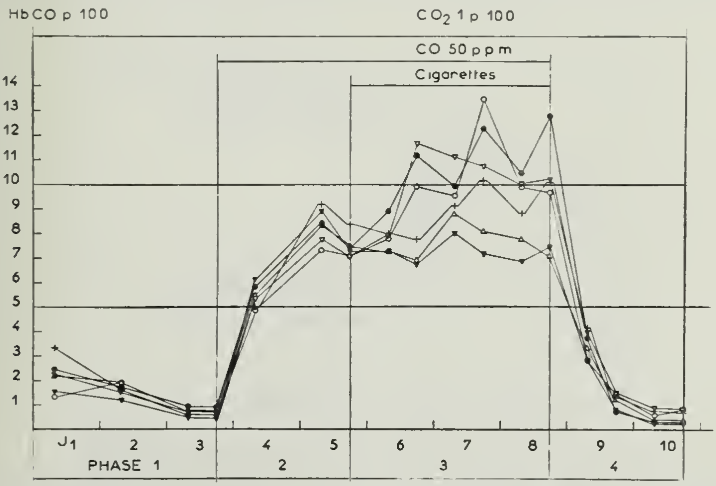

Fig. 1. Évolution du pourcentage de Hb CO au cours des différentes phases de l'expérience

des fumeurs modérés (valeurs initiales d'Hb CO comprises entre 1,5 et 3 pour cent), dès qu'ils cessent de fumer dans une atmosphère sans CO, les taux d'Hb CO s'abaissent et se stabilisent entre 0 et 1 pour cent au bout de 48 h (oxycarbonémie endogène).

Après cette phase de désintoxication, le séjour dans une atmosphère à 50 ppm de CO (phase 2) amène les valeurs d'Hb CO à un plateau compris entre 8 et 10 pour cent en une trentaine d'heures; cette valeur est en accord avec la littérature de même que la valeur de 14 à 15 pour cent que nous avons observée lors d'un séjour dans une atmosphère à 100 ppm de CO (phase 2 de l'expérience III).

Dans la phase suivante, les sujets toujours soumis à 50 ppm de CO ont eu la permission de fumer, le taux d'Hb CO augmente alors et pour une consommation de 10 à 20 cigarettes par jour se trouve compris entre 9 et 15 pour cent. La dispersion visible sur la figure dépend, rappelons-le, de la quantité de cigarettes fumées et de la façon de fumer. Notons que cette valeur de 15 pour cent correspond approximativement à celle qui est observée lors du séjour dans une atmosphère contenant 100 ppm de CO.

Dès que les sujets cessent de fumer mais restent soumis à 50 ppm de CO, le pourcentage d'Hb CO diminue lentement et se stabilise à 8–9 pour cent (Phase 3 de l'expérience III).

Influence de CO *et du Tabac sur les Paramètres Cardio-respiratoires*

Les mesures ont été pratiquées au repos, pendant le travail et pendant la phase de récupération.

Au repos. Le débit et la fréquence respiratoire, la consommation d'oxygène, ne sont pas affectés lors des différentes phases des expériences (CO seul, CO et tabac).

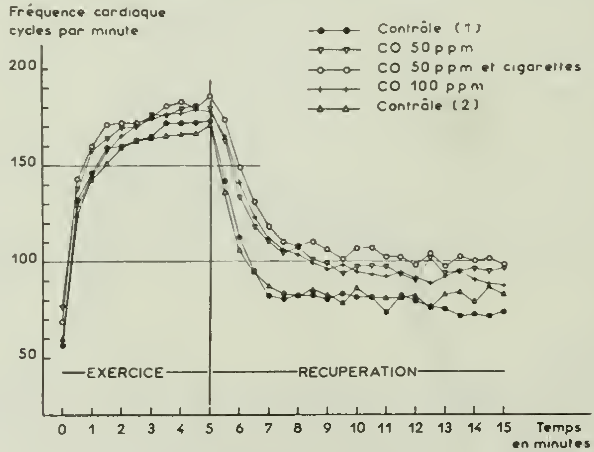

FIG. 2. Courbe type (sujet No 3) des fréquences cardiaques à l'effort au cours des différentes phases de l'expérience 3

La fréquence cardiaque augmente légèrement chez la plupart des sujets pendant la phase CO seul et la phase CO et tabac.

Au cours du travail. Le débit et la fréquence respiratoire, la consommation d'oxygène ne sont pas affectés par le CO et le tabac. La fréquence cardiaque augmente chez tous les sujets lorsqu'ils sont soumis à 50 ppm de CO (augmentation moyenne de 7/min). A 100 ppm ou à 50 ppm et cigarettes, l'augmentation moyenne est plus importante (16/min).

Au cours de la récupération. Le débit et la fréquence respiratoire, la consommation d'oxygène ne varient pas. Par contre, la fréquence cardiaque augmente significativement chez tous les sujets: (Fig. 2) 7/min pour 50 et 100 ppm, pour 50 ppm et cigarettes, l'augmentation moyenne est de 18/min.

L'adaptation circulatoire à l'exercice est moins bonne et la récupération se fait moins bien chez les sujets soumis à une atmosphère contenant du CO aux concentrations de 50 et 100 ppm ; si les sujets fument dans cette atmosphère, l'effet est notablement augmenté.

Influence de CO *et du Tabac sur l'Acuité Visuelle Nocturne*

Les résultats indiquent que le S.M.E. ne semble pas être particulièrement dégradé chez les sujets exposés à 50 ppm et 100 ppm de CO (Hb CO respectivement 8 et 15 pour cent), par contre si les sujets fument 15 à 20 cigarettes par jour dans une atmosphère à 50 ppm de CO (ce qui fait passer le taux d'Hb CO de 8 à 15 pour cent), on note alors une dégradation nette du seuil morphoscopique élémentaire statistiquement très significative (0,2 U.L.) (Fig. 3, IIIème phase).

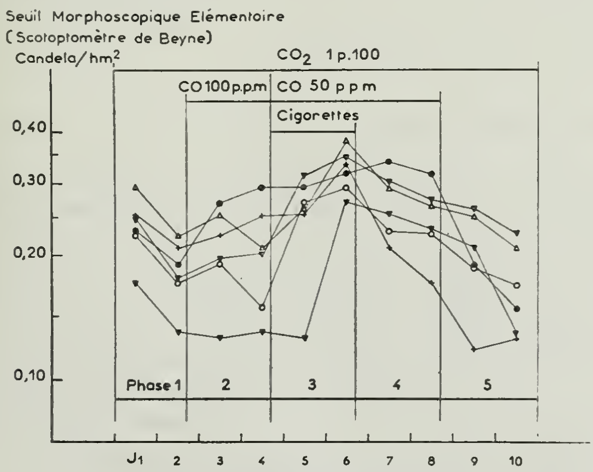

Fig. 3. Evolution des valeurs du seuil morphoscopique élémentaire en unité logarithmique candela/hm2 au cours des différentes phases de l'expérience 3

DISCUSSION

Paramètres Cardio-respiratoires au Cours de l'Effort

L'absence de variations des paramètres respiratoires au cours de l'effort musculaire intense (consommation d'oxygène 3 l./min) avec des valeurs d'Hb CO de 8 à 15 pour cent est conforme aux données de la littérature et notamment aux résultats d'Asmussen (1943) (pas de variation pour un travail de 720 kg/min avec des valeurs d'Hb CO atteignant 20–30 pour cent) et d'Apthorp (1958). Par contraste, Astrand (cité par Dejours (1959) observe des variations du débit respiratoire de 100 pour cent pour un travail nécessitant une consommation d'oxygène de 3 l./min à une altitude de 4000 m entrainant une désaturation de l'oxyhémoglobine de 15 pour cent. Ces différences observées dans les résultats de l'intoxication oxycarbonée légère et l'hypoxémie d'altitude s'expliquent facilement par le rôle de la pression partielle d'oxygène sur les chémorécepteurs.

L'augmentation de la fréquence cardiaque au cours de l'effort et surtout au cours de la phase de récupération chez les sujets sous CO a déjà été signalée (Asmussen, 1941; Apthorp, 1958; Dahlström, 1947) mais n'a jamais été mise en évidence pour des valeurs d'Hb CO aussi faibles (8–15 pour cent). Il est vrai que les sujets dans nos expériences étaient soumis à un travail particulièrement intense qui exigeait une intégrité de la capacité de transport d'oxygène dans le sang. Afin de savoir si le tabac agit seulement par le CO auquel il donne naissance, les sujets dans la dernière expérience ont été soumis dans une phase à 100 ppm de CO, sans tabac, et dans une autre phase à 50 ppm de CO avec tabac, de telle façon que les pourcentages d'Hb CO soient voisins. L'augmentation de la fréquence cardiaque nettement plus importante observée dans la phase 50 ppm et tabac semble indiquer une action défavorable propre au tabac (nicotine ou autres facteurs), sur l'adaptation et la récupération lors d'une exercice musculaire.

Hb CO, *Tabac et Vision Nocturne*

Les rares travaux effectués sur les effets de l'oxycarbonémie modérée sur la vision nocturne au cours de brèves inhalations de CO (Abramson et Heyman, 1944, Scobee et Chinn) montrent en accord avec nos résultats obtenus lors d'expositions de longue durée une corrélation faible et inconstante. Par contre, nos résultats mettent en évidence de façon certaine (3ème phase, Fig. 3) une action défavorable de la fumée de tabac indépendante du taux d'oxycarbonémie; cette action a déjà été observée et diversement interprêtée, Mac Farland *et coll.* (1944) l'attribue au CO ce que nos propres résultats infirment, tandis que Sheard (1946) estime que la nicotine en est responsable. Il est difficile en l'absence d'expérimentation systématique (utilisation de cigarettes sans nicotine) de se prononcer sur l'importance de tel ou tel composant de la fumée de tabac, CO exclu.

CONCLUSIONS

(1) Les taux de carboxyhémoglobine de 9 et 15 % correspondant à des expositions prolongées à des concentrations respectivement de 50 et 100 ppm CO n'entrainent aucune variation des réactions respiratoires à l'effort mais provoquent par contre une augmentation significative de la cardio-accélération au cours de l'effort et de la phase de récupération; l'adaptation circulatoire à l'exercice est moins bonne et la récupération se fait moins bien.

(2) Ces taux de carboxyhémoglobine n'amènent que des variations faibles et inconstantes de la vision nocturne (seuil morphoscopique élémentaire).

(3) Les sujets exposés à une atmosphère contenant 50 parties par million de CO et fumant 15 à 20 cigarettes par jour élèvent leur taux de carboxyhémoglobine jusqu'à 15 pour cent. Dans ces conditions on observe une augmentation de la cardio-accélération au cours du travail plus importante que ne le ferait prévoir l'oxycarbonémie correspondante. Parallèlement, le seuil morphoscopique visuel nocturne est très significativement augmenté. Ces faits semblent prouver une action propre du tabac indépendante de l'oxycarbonémie.

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RESPIRATORY CHANGES AND CARBON DIOXIDE EFFECTS UNDER HIGH PRESSURE

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Abstract – Retention of carbon dioxide by working divers at depth can be expected when increased gas density produces a critical increase in respiratory work. In some divers, inadequate ventilation is observed even under apparently favorable conditions. CO_2 retention appears capable of producing increased susceptibility to oxygen poisoning and of intensifying the narcotic effects of nitrogen. Increased respiratory work and CO_2 effects can be expected to influence the maximum practical depth of diving with gaseous breathing media.

Zusammenfassung – Bei Tauchern, die unter Wasser arbeiten, kann man eine CO_2-Retention dann erwarten, wenn die zunehmende Gasdichte einen kritischen Anstieg der Atemarbeit bewirkt. Bei einigen Tauchern wurde jedoch eine unzureichende Ventilation schon unter Bedingungen beobachtet, die nach objektiven und subjektiven Kriterien sonst als günstig anzusehen waren. Die CO_2-Retention scheint die Empfindlichkeit gegenüber den toxischen Wirkungen des Sauerstoffs und die narkotische Wirkung des Stickstoffs zu verstärken. Die vermehrte Atemarbeit und diese CO_2-Wirkungen sind vermutlich die Faktoren, die beim Tauchen die praktisch erreichbare maximale Tiefe begrenzen, solange gasförmige Medien geatmet werden.

Résumé – On peut prévoir une rétention de gaz carbonique chez les plongeurs au travail lorsque l'augmentation de la densité gazeuse produit une augmentation critique du travail respiratoire. Pourtant, on observe une ventilation insuffisante. Chez certains plongeurs même dans des conditions qui sembleraient, de prime abord, favorables. La rétention de CO_2 semble augmenter la sensibilité à l'empoisonnement par l'oxygène et intensifier les effets anesthétiques de l'azote. L'augmentation du travail respiratoire et les effets du gaz carbonique exercent une influence sur la profondeur de plongée maxima.

WITH the increasing pressure of depth in diving, the work of breathing increases with the greater density of respired gas (Marshall, Lanphier and DuBois, 1956; Buehlmann, 1963; Lanphier, 1963). The consequences are reflected in decreasing maximum breathing capacity (MBC). Several independent studies have shown, for example, that MBC is approximately halved in going from normal pressure to 4 atm abs. (99 ft or 30 m of sea water); that beyond 3 atm the decrease continues but at a lesser rate (Miles, 1957; Seusing *et al.*, 1960; Wood, 1963). Wood (1963) reported MBC values approximately $^1/_4$ normal at 15 atm breathing air. The effort required for quiet resting respiration apparently does not become prohibitive until very great depths are reached, but severe limitation of exercise ventilation can be expected.

The limits have not yet been defined adequately, but it appears doubtful that the respiratory needs of moderate exertion can be met comfortably with air at pressures much beyond 4 atm abs. When the limits of practical ventilatory capacity are exceeded, retention of CO_2 becomes inevitable if a diver continues exertion at an excessive rate. The use of gases less dense than air offers considerable extension of the limits. For example, Wood (1963) found that an 80–20 He–O_2 mixture yielded about the same MBC at 10 atm as was achieved with air at 4 atm. With 95–5 He–O_2, this value was maintained at 15 atm. Despite such gains, it appears certain that reduced ventilatory capacity will prohibit useful degrees of exertion at extreme depths. However, it is not yet clear whether this or one of the other serious problems of deep diving will set the ultimate limit of practical depth.

Common experience suggests that dyspnea would provide ample warning of significant retention of CO_2 and that this would not occur if an adequate reserve of ventilatory capacity remained. However, my own studies at the U.S. Naval Experimental Diving Unit (E.D.U.) revealed that inadequate ventilation and CO_2 retention occur during exertion in certain healthy, experienced divers even when the work of breathing is neither objectively nor subjectively excessive (Lanphier, 1956). Similar findings have been reported by Goff and Bartlett (1957) in underwater demolition personnel (frogmen). The ventilatory deficiency of the divers was increased with elevation of inspiratory oxygen pressure and with added respiratory work, but abnormal elevations of alveolar and arterial CO_2 tension were observed during moderate exertion even when breathing air at normal pressure with a respiratory circuit having negligible resistance. At no time was CO_2 retention associated with complaints of dyspnea. The basic problem appeared to be an abnormality of respiratory control. Grossly subnormal respiratory responses to inspired CO_2 were demonstrated, suggesting a form of adaptation similar to that reported by Schaefer in submarine escape training personnel (1963). Much remains to be learned about this phenomenon and its implications in deeper diving.

Accelerated onset of oxygen convulsions is a long-recognized effect of adding CO_2 to the inspired gas under increased pressure, and it is reasonable to expect that CO_2 retention would have similar consequences under conditions where oxygen poisoning is possible. Unusual susceptibility to oxygen poisoning when breathing nitrogen–oxygen mixtures at depth was the problem that caused us to investigate the adequacy of ventilation in E.D.U. divers. The relationship between CO_2 retention and the effect of exertion upon oxygen toxicity remains to be clarified. Lambertsen (1959) suggests the interesting possibility that exertion may shorten the latent period only in men who retain CO_2.

The role of CO_2 retention in nitrogen narcosis is a subject of recurrent controversy. My own observations indicate that typical narcotic effects appear when there is no evidence of CO_2 retention, and I am obliged to conclude that nitrogen has distinct narcotic properties of its own. However, we have experienced very marked accentuation of effects when CO_2 retention is induced in the presence of narcosis, as by exertion with inadequate pulmonary ventilation when breathing air at 7.8 atm.

Elevations of P_{CO_2} which produced coma under those conditions had little or no mental effects when induced in the absence of nitrogen. These findings are in accord with conclusions reached by Case and Haldane (1941). The subjects of these recent studies have experienced extreme dyspnea with CO_2 levels that enhanced narcosis significantly during exertion. In them, avoidance of exertion producing dyspnea would apparently prevent serious accentuation of narcosis. However, it is by no means certain that this would be the case in divers with a pronounced tendency to retain CO_2. The studies in E.D.U. divers did not shed light on this question since the nitrogen levels of exposure were relatively low and symptoms of narcosis were not reported even when alveolar P_{CO_2} exceeded 60 mm Hg.

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EFFECT OF EXPOSURE TO INCREASED PRESSURE ON ARTERIAL ALVEOLAR P_{O_2}, P_{CO_2} AND P_{N_2} DIFFERENCES*

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Abstract – The AaD_{O_2}, N_2 and CO_2 have been measured at two different levels (sea level 2.6 Atm) of surrounding pressure. The data shows that most of the AaD_{O_2} is caused by uneveness of the ventilation to perfusion rations. Only a small part of the total O_2 difference corresponds to a real shunt which cannot be calculated at sea level conditions. The data also suggests that in some subjects a long exposure to a high P_{O_2} might impair the $\dot{V}_A/Q$ distribution.

Zusammenfassung – Der AaD_{O_2}, N_2 und CO_2 wurde bei zwei verschiedenen Umgebungsdrucken gemessen. Die Ergebnisse zeigen, dass der grösste Teil der alveoloarteriellen Differenz für O_2 bedingt ist durch das ungleiche Verhältnis zwischen Belüftung und Durchblutung der Lunge. Nur ein kleiner Anteil der gesamten AaD_{O_2} entspricht einem wirklichen shunt, der unter normalen Druckverhältnissen nicht berechnet werden kann. Weiter weisen die Ergebnisse darauf hin, dass ein langer Aufenthalt bei hohem P_{O_2} die V_A/Q Verteilung schädigen kann.

Résumé – AaD_{O_2}, N_2 et CO_2 ont été mesurés à deux pressions ambiantes différentes, c'est à dire au niveau de la mer et à 2,6 Atm. Les résultats montrent que la plus grande partie de AaD_{O_2} est due à l'inégalité des rapports entre la ventilation et la perfusion. Seule une petite part de AaD_{O_2} est causée par un shunt réel qui ne peut être mesuré à la pression barométrique existant au niveau de la mer. Les résultats laissent supposer qu'une exposition prolongée à une pression d'O_2 élevée altére la distribution de V_A/Q.

It is well known that normal subjects breathing room air at sea level have a difference in partial pressure of O_2, CO_2, and N_2 between the mixed alveolar gas and the mixed arterial blood. The alveolar arterial differences, AaD, for these gases result from three factors. These factors vary in their effect upon the AaD for each gas (Fig. 1).

The first and the least important of these factors is a diffusion barrier. It creates a negligible AaD for O_2 in normal subjects and does not prevent CO_2 and N_2 from reaching complete equilibrium.

The second factor is an anatomical shunt. It is responsible for a AaD in O_2 whose size depends on the size of the shunt, but it cannot cause an AaD_{N_2} since the partial pressure in N_2 is the same in the arterial and venous blood. Also, a shunt that does not exceed 10 per cent of the cardiac output causes only a negligible AaD_{CO_2}

The third factor is an uneveness of the ventilation/perfusion ratio $\dot{V}_A/\dot{Q}$

* Supported by The American Thoracic Society, National Tuberculosis Association.

throughout the lung. This factor is responsible for an AaD in O_2, CO_2 and N_2 since the alveolar air and the arterial blood coming from units with a different ventilation/perfusion ratio do not have the same gas partial pressures. If the relationship between the blood gas content and the partial pressure of all gases was linear, the P_{O_2}, difference resulting from a variance in $\dot{V}_A/\dot{Q}$ would be equal and opposite to the sum of the P_{CO_2} and P_{N_2} differences. However, since the O_2 and CO_2 dissociation curves are not linear over the pressure range found in the alveoli at sea level, the P_{O_2} difference is always larger than the sum of the two others (Lenfant, 1963).

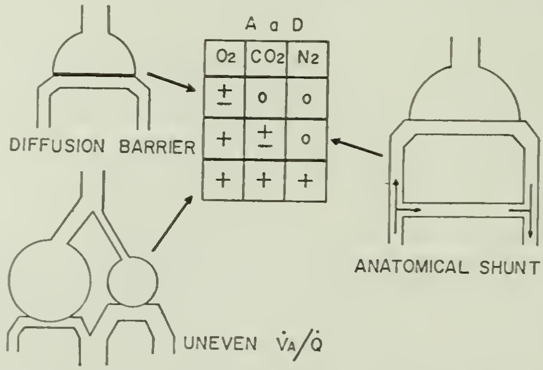

FIG. 1. Alveolar-arterial differences AaD in P_{O_2}, P_{CO_2} and P_{N_2} related to three factors: (1) diffusion barrier (2) anatomical shunt (3) uneven $\dot{V}_A/\dot{Q}$ (schematic)

Let us see what can theoretically happen to the AaD due to these three factors when: (1) the fraction of O_2 in the inspired gas is raised to 75 per cent at sea level (2) the barometric pressure is increased to 2.6 atm and when the subject breathes 75 per cent O_2.

The diffusion barrier can be eliminated as a cause of AaD at sea level and at increased barometric pressure when normal subjects breathe 75 per cent O_2. In these two conditions the driving pressure for O_2 is high enough and the reaction time between O_2 and hemoglobin is fast enough to secure complete equilibrium on both sides of the alveolar membrane.

The P_{O_2} difference resulting from an anatomical shunt is affected by a change in partial pressure of O_2 in the alveolar gas (Fig 2). In the pulmonary circulation, most of the blood (or capillary blood) is exposed and equilibrated with the alveolar P_{O_2} and only a small amount of blood (or shunted blood) keeps a venous O_2 content ($C_{\bar{v}}$). When these two bloods merge the resulting mixed blood has an O_2 content $C_{\bar{a}}$ slightly smaller than the O_2 content of the capillary blood Cc. This difference in O_2 content corresponds to a difference in P_{O_2}, between the mixed alveolar air and the mixed arterial blood that varies with the absolute value of P_{O_2}, in the alveolar gas.

As shown in the upper graph of Fig. 2, at sea level, breathing room air the resulting AaD_{O_2} is very small because of the steep slope of the O_2 dissociation curve.

As seen in the middle graph of Fig. 2, at sea level, with an F_{O_2} of 75 per cent the P_{O_2}, in the alveolar gas increases. Also the slope of the O_2 dissociation curve be-

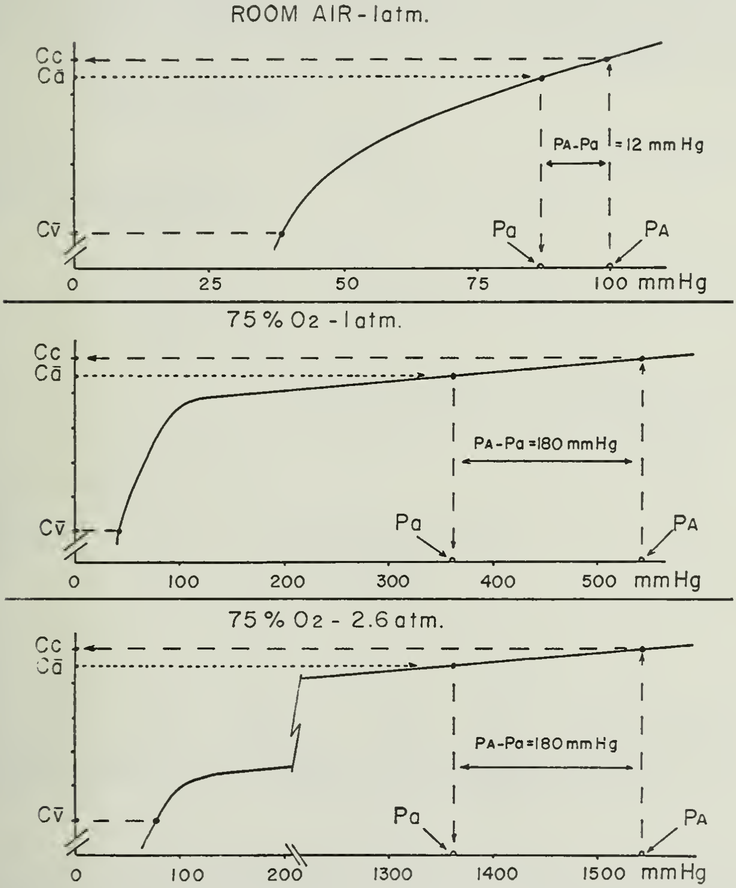

Fig. 2. Theoretical effects of increase in inspired P_{O_2} and total barometric pressure on AaD_{O_2} assuming that anatomical shunt and arterial venous difference in O_2 do not change

comes more gradual since only dissolved oxygen is added to the blood. Then if the size of the shunt remains the same, the difference in O_2 content between the capillary blood and the mixed arterial blood remains the same also, but the corresponding difference in P_{O_2}, becomes much larger.

When the barometric pressure is raised, P_{O_2} increases proportionally in the alveolar gas and therefore more oxygen is dissolved in the capillary blood, but as shown in the lower graph of Fig. 2 the shape of the upper part of the O_2 dissociation curve is not affected, since it is a linear relation depending only on the solubility of O_2. Then the same shunt creates the same AaD_{O_2} as that at sea level even if the absolute values are much higher.

One can therefore see that when the barometric pressure is raised the AaD_{O_2} is not affected, provided that neither the size of the shunt nor the arterial venous difference in O_2 change.

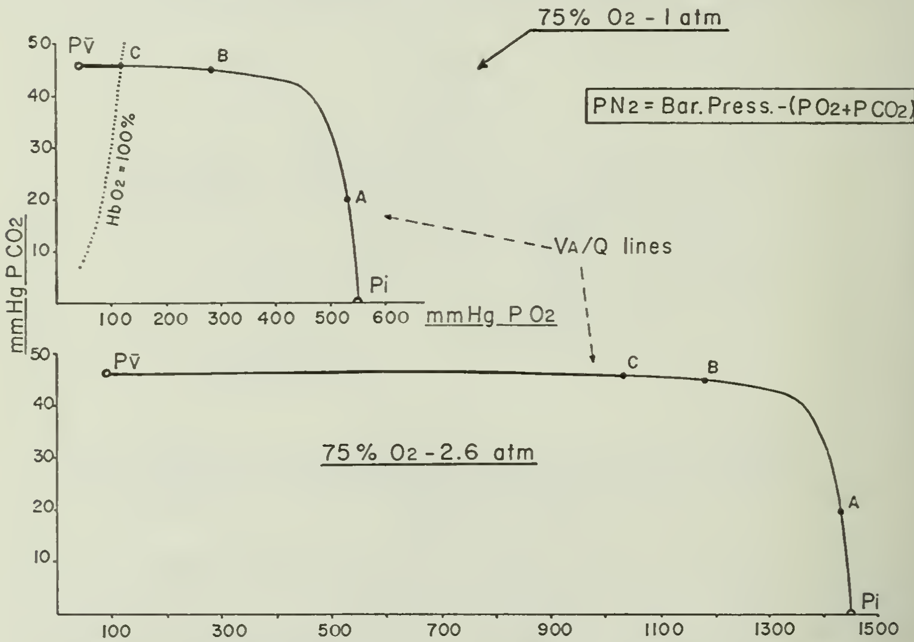

FIG. 3. Effects of changes in barometric pressure while breathing 75 per cent CO_2 on ventilation/perfusion ratios presented in the O_2–CO_2 diagram (theoretical)

In regard to an uneveness of the ventilation/perfusion ratio the effect of a change in barometric pressure when breathing 75 per cent O_2 can be represented on an O_2–CO_2 diagram (Fig. 3).

On this diagram having P_{O_2} and P_{CO_2} as coordinates, all the parameters pertaining to the gas exchange are shown. Between the two extremes, inspired gas P_I and venous blood gas pressure $P_{\bar{v}}$ lies a line corresponding to all the possible ventilation/perfusion ratios existing in the lung. For each point on this line the difference between the barometric pressure and the sum of P_{O_2}, and P_{CO_2} is equal to the partial pressure in N_2. Also an alveolus, such as B, with a low P_{O_2} has a high P_{CO_2} and a high P_{N_2}; inversely an alveolus A with a high P_{O_2} has a low P_{CO_2} and a relatively lower P_{N_2}. When the barometric pressure is increased to 2.6 atm the difference in P_{O_2} between the venous blood and the inspired gas becomes much greater because of the huge increase of the amount of dissolved O_2. However, only that part of the $\dot{V}_A/\dot{Q}$ line corresponding to alveoli that do not saturate the blood at ambient pressure increases; this portion of the $\dot{V}_A/\dot{Q}$ line lies between the points $P_{\bar{V}}$ and C.

Since the gradients result from the dispersion of the gas partial pressures throughout the lung, it is important to consider whether the dispersion is affected by the raise in barometric pressure. Figure 4 shows* that if there are only alveoli with

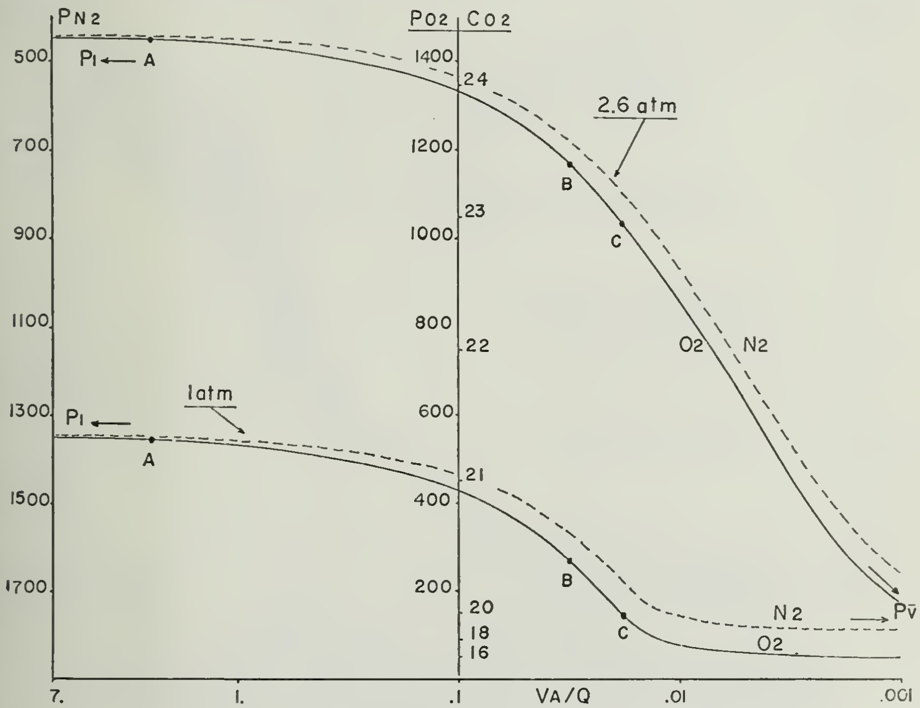

FIG. 4. Effects of increased pressure on gas partial pressures in alveoli with different $\dot{V}_A/\dot{Q}$ ratios (theoretical)

a $\dot{V}_A/\dot{Q}$ ratio such as A and B, the absolute value of the gas pressure increases but not the dispersion. Inversely if there are alveoli with so low a $\dot{V}_A/\dot{Q}$ that they do not saturate the blood at ambient pressure (between C and P_V) the dispersion in P_{O_2} and P_{N_2} is considerably increased. As seen on Fig. 4 these alveoli must have a $\dot{V}_A/\dot{Q}$ lower than 0.016. Such a $\dot{V}_A/\dot{Q}$ corresponds to unventilated alveoli or to gas pockets.

As an example, Fig. 5 shows the AaD that would result from a $\dot{V}_A/\dot{Q}$ distribution in which a large compartment (90 per cent of the lung) is well ventilated, and a small compartment is poorly ventilated as compared to its blood flow. If $\dot{V}_A/\dot{Q}$ of

* The vertical distance between PO_2 and PN_2 lines at both pressures corresponds to PCO_2.

the small compartment is higher than 0.016 the change in barometric pressure has no effect on the O_2 and N_2 difference. If $\dot{V}_A/\dot{Q}$ of this compartment is smaller than 0.016 the larger dispersion in P_{N_2} resulting from the increase in barometric pressure causes AaD_{N_2} to increase considerably. The O_2 difference is also affected but toward a decrease. This is due to the fact that the effect of the O_2 dissociation curve is eliminated because of the large amount of dissolved oxygen.

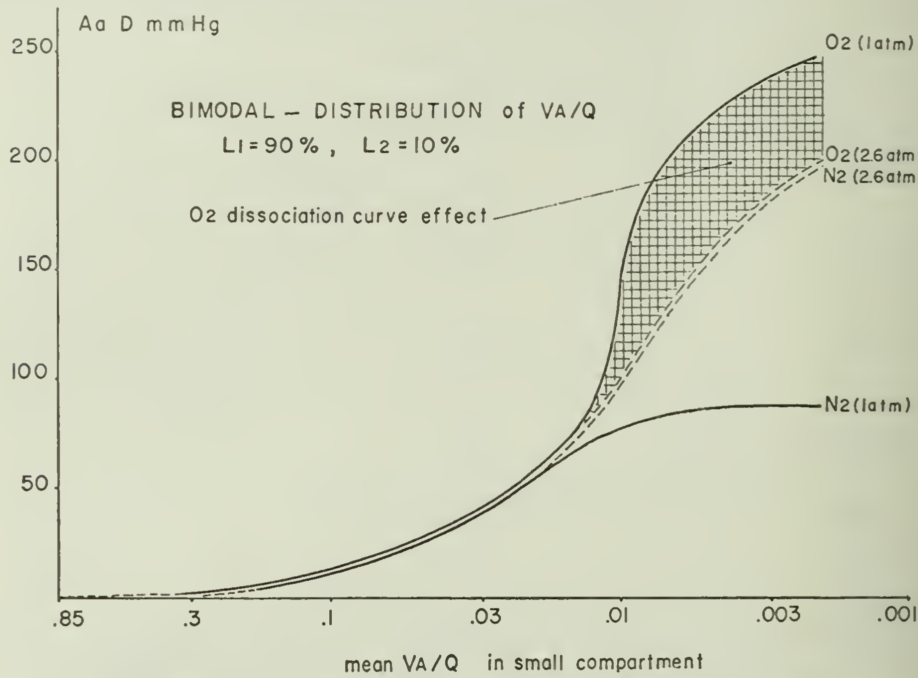

FIG. 5. Effects of increased pressure on $AaDO_2$ and N_2 at a $\dot{V}_A/\dot{Q}$ distribution of a large well ventilated compartment (90 per cent of the lung) and a small poorly ventilated compartment (10 per cent) (theoretical)

Then one can see that the effect of an increase in barometric pressure on AaD_{O_2} and AaD_{N_2} due to an uneven distribution of $\dot{V}_A/\dot{Q}$ depends only upon the type of distribution. If the distribution is such that all alveoli can secure a complete saturation of the dependent blood there is no change in the AaD, but if the distribution is so scattered that some alveoli do not saturate the blood at sea level when breathing 75 per cent O_2, the AaD_{N_2} increases and AaD_{O_2} decreases as the barometric pressure is elevated.

To test the role played by each of the two main factors the AaD in O_2, CO_2 and N_2 have been measured in eight professional divers of the U.S. Navy, breathing 75 per cent O_2 at sea level and at 2.6 atm. P_{O_2} and P_{CO_2} in the arterial blood were measured by standard electrometric methods; P_{N_2} in blood and all the alveolar gas pressures were measured by gas chromatography. The results showed three different patterns for the change in the AaD with the change in barometric pressure (Fig. 6).

In one subject all the (Aa)D remained the same for all the gases. Then no change in the shunt and in the $\dot{V}_A/\dot{Q}$ distribution occured. Also the $\dot{V}_A/\dot{Q}$ distribution in this subject included only alveoli that secured complete saturation at both pressures.

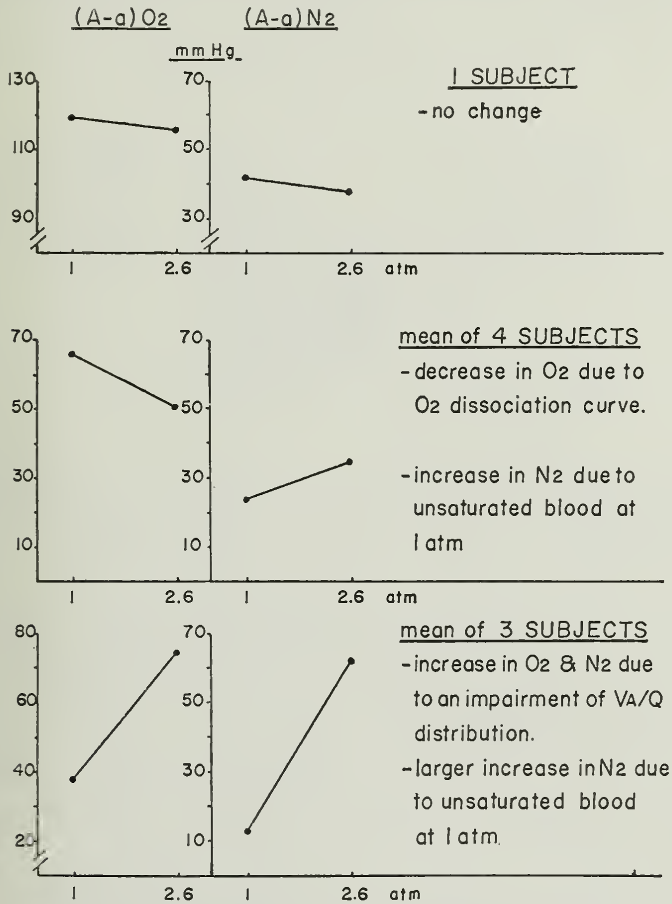

Fig. 6. Measured (alveolar-arterial) O_2 and N_2 gradients in 8 Navy divers breathing 75 per cent O_2 at sea level and 2.6 atm, showing three different patterns of response

Four subjects had an increase of their AaD_{N_2} and decrease of the O_2 difference. This can be explained by a distribution of the ventilation/perfusion ratios that include alveoli which did not saturate the blood at sea level, i.e. had a $\dot{V}_A/\dot{Q}$ lower than 0.016. Three subjects had an increase of AaD_{O_2} and AaD_{N_2} but the N_2 difference increased more than the O_2 difference. This pattern shows that these subjects had a distribution including alveoli that did not saturate the capillary blood at sea level, similar to the group of 4 subjects above. It also shows that the number of these alveoli increased for some unknown reason at the higher barometric pressure.

As shown previously, the total AaD_{O_2} is only composed of the shunt and of the distribution component since the diffusion factor is negligible if nonexistent. The distribution component is best represented by the sum of the CO_2 and N_2 difference, then at least a part of the total AaD_{O_2} equal to this sum is due to the distribution factor. What is left of the total O_2 difference is due to the shunt component and only this part should be used to calculate the real shunt (Fig. 7).

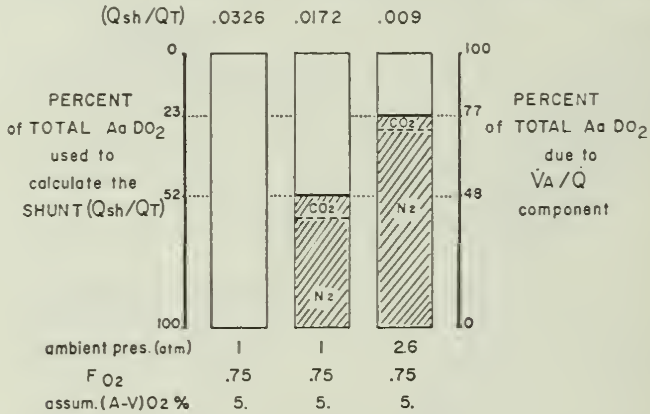

FIG. 7. Partition of alveolar-arterial pO_2 difference in 2 components: 1) $\dot{V}_A/Q$ distribution = sum of CO_2 and N_2 differences, 2) Anatomical shunt component = $AaD_{O_2} - (AaD_{N_2} + AaD_{CO_2})$. Mean of 7 professional divers

However, since we have shown there are alveoli with a very low $\dot{V}_A/\dot{Q}$ that do not saturate the capillary blood at sea level even when breathing 75 per cent O_2, the shape of the O_2 dissociation curve enhances the O_2 gradient due to distribution.

Therefore, under these conditions the part of the total AaD_{O_2} due to real shunt is most likely to be less than the difference between the total AaD_{O_2} and the sum of AaD_{N_2} and AaD_{CO_2}.

At 2.6 atm, with $F_{O_2} = 75$ per cent, the magnifying effect of the O_2 dissociation curve is eliminated since there is so large an amount of dissolved oxygen that the venous blood remains almost fully saturated. In such circumstances, the two main factors, shunt and distribution can be really separated, and it is seen that only a quarter of the total AaD_{O_2} is caused by the anatomical shunt.

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EFFECTS OF BUFFERS ON ACUTE AND SUBACUTE OXYGEN TOXICITY IN RODENTS

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THERE has been much discussion of the possible role played by free CO_2 accumulation in the toxicity observed during exposure to high oxygen tensions. Studies have been made of the effect of THAM (tris(hydroxymethyl)aminomethane) administration on O_2 toxicity in mice (Nahas and Sanger, 1961; Sanger and Nahas, 1961; Sanger *et al.*, 1961). Thirty minutes after a single intraperitoneal injection of 1 ml of 0.3M THAM, the mice were exposed to 30, 42 and 55 psi O_2. There was a significant delay in the appearance of convulsions. This delay did not occur after a single injection of 0.3M $NaHCO_3$. However, 3 injections of 0.3M THAM or 0.3M $NaHCO_3$ administered over a 6-hr period were equally effective. Oxygen toxicity, therefore, may be associated with acid-base imbalance which can, to some extent, be alleviated by the administration of buffers. The exact nature of the acid-base imbalance and its correction is still to be determined. Bean (1961) made similar observations in rats, exposed to 80 psi of O_2 8 to 10 min after the injection of a 10 per cent solution of THAM (1.5 g/kg) in isotonic saline solution. THAM postponed the onset of seizures and decreased their incidence and severity. Lung damage was either absent or much less severe than in control animals, and mortality rate was lower (14 per cent instead of 38 per cent). Bean suggested that such highly significant ($P < 0.01$) results should redirect attention toward increased tissue P_{CO_2} and tissues $[H^+]$ as possible contributors to the toxic reaction to high oxygen pressures.

Kylstra (personal communication) also observed that a single intraperitoneal injection of 0.3M THAM significantly protected mice against convulsions and neurological damage following exposure to 8 atmospheres of oxygen.

Matteo (Matteo and Nahas, to be published), in our laboratory, has shown that treatment of rats with daily injections of 0.15 M sodium bicarbonate administered intraperitoneally (dosage 50 ml/kg) significantly decreased the mortality rate of animals exposed to pure oxygen at atmospheric pressure during 4 weeks. Animals treated with THAM had a mortality rate similar to that of control. The hypoglycemic effect of this compound might be the cause for its lack of effect when administered daily. Bicarbonate did not prevent degenerative testicular changes which started developing in these animals 8 days after exposure to pure oxygen.

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ADAPTATION TO CO_2 WITH PARTICULAR RELATION TO CO_2 RETENTION IN DIVING

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Abstract – Adaptation to CO_2 produces a typical breathing pattern of increased tidal volume and lowered respiratory rate. Anatomical and physiological deadspace, as well as arterial-alveolar CO_2 and O_2 gradients, are increased under these condions. The relationship of these findings with the well known lowered respiratory response to high CO_2 concentrations after CO_2 adaptation is discussed. Evidence for CO_2 adaptation in routine diving is presented.

Zusammenfassung – Die Anpassung an längerdauernde Kohlensäure Einwirkung äussert sich in einem typischen Atmungsrhythmus mit erhöhtem Atemvolumen und verminderter Atemfrequenz. Der anatomische und physiologische Totraum ist vergrössert und der AaD_{CO_2} und AaD_{O_2} erhöht. Die Beziehung dieser Befunde zu der bekannten verminderten Reaktion der Atmung bei Einatmung hoher CO_2 Konzentrationen nach CO_2 – Adaptation wird diskutiert. Es werden Befunde berichtet, die beweisen, dass Kohlensäureadaptation bei regelmässigem Tauchen auftritt.

Résumé – L'acclimatation à l'absorption de CO_2 pour une longue durée se traduit par une augmentation du volume d'air inspiré et une réduction de la fréquence respiratoire. Les temps-morts anatomique et physiologique ainsi que les gradients artérioalvéolaires en CO_2 et O_2 sont augmentés. On discute les relations existant entre ces resultats et le fait bien connu que le système respiratoire devient moins sensible au gaz carbonique après acclimatation à l'hypercapnie. Il est en outre démontré qu'il y a adaptation au CO_2 dans le cas de plongées régulières.

It has been established that prolonged exposure to increased CO_2 concentration results in a reduction of the ventilatory response to CO_2 (Haebisch, 1949; Schaefer, 1949; Chapin, 1955). CO_2 tolerance curves obtained after three days of exposure to 3 per cent CO_2 showed a shift to the right and a decrease in slope (Schaefer, 1949). During acclimatization to 3 per cent CO_2, the tidal volume increased and respiratory rate decreased (Schaefer, 1949) which suggested that the respiratory pattern is an important factor in the respiratory response to CO_2. Studies of acute exposure to various CO_2 concentrations on a large group of subjects established clearly the relationship of respiratory pattern and ventilatory response to CO_2. Subjects with a large tidal volume and a low frequency showed a significantly lower response to CO_2 than those with a small tidal volume and high respiratory rate (Schaefer, 1958) (Fig. 1).

Subjects were classified in a low and high ventilation group, using as criteria a ventilation ratio of 4 at 5.4 per cent CO_2 and 6 at 7.5 per cent CO_2. For example, subjects who responded to the inhalation of 5.4 per cent CO_2 with an increase in respiratory minute volume less than four times the basic volume on air were grouped in the low ventilation group. By comparing the CO_2 tolerance curves of the low and high ventilation groups with those collected under conditions of adaptation to prolonged exposure to 3 per cent CO_2 (Fig. 2), it was concluded that the low ventilation group had to be considered adapted in normal life to a higher CO_2 level.

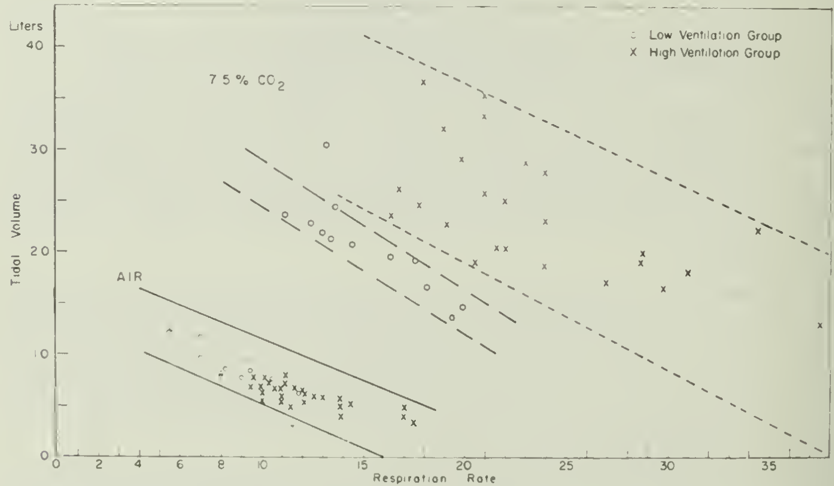

FIG. 1. Relationship between respiratory rate and tidal volume breathing air and breathing 7.5 per cent CO_2
o Low ventilation group
x High ventilation group.
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Supporting evidence for this notion was obtained in a study of 21 subjects exposed to 1.5 per cent CO_2 for 42 days (Schaefer *et al.*, 1963). Figure 3 shows changes in respiratory pattern during acclimatization to 1.5 per cent CO_2. Tidal volume increased markedly throughout exposure and remained high for nine days of recovery, while respiratory rate declined after initial transitory rise. Increase in respiratory minute volume, produced by exposure to 1.5 per cent CO_2, amounted to 34–38 per cent and was mainly accomplished through change in tidal volume.

Throughout exposure to CO_2 anatomical dead space was increased and alveolar ventilation, expressed in per cent of total ventilation, was correspondingly decreased.

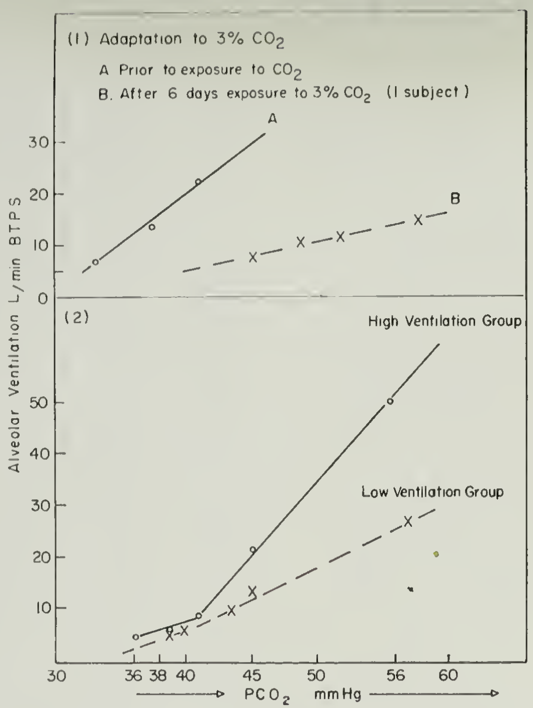

Fig. 2. CO_2 ventilation response 1. During adaptation to 3 per cent CO_2 and 2. of the high and low ventilation groups. Printed with permission of the *Journal of Applied Physiology*

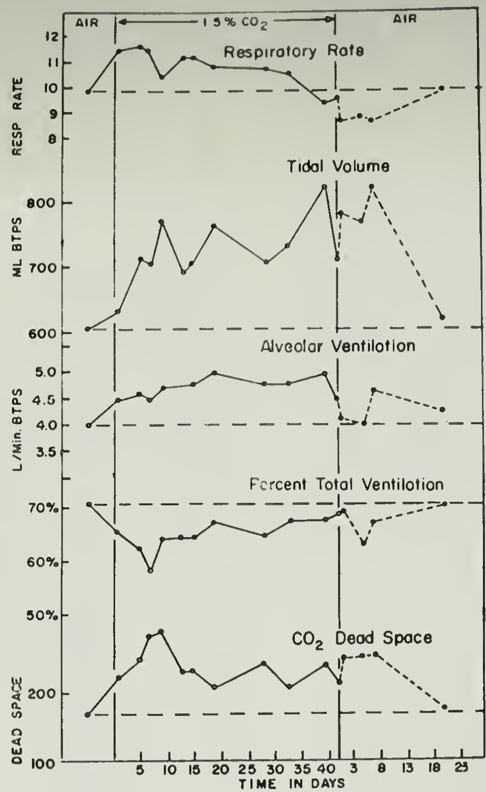

Fig. 3. Effect of prolonged exposure to 1.5 per cent CO_2 on respiratory rate, tidal volume, alveolar ventilation and anatomical deadspace. (Mean values 21 subjects). Printed with permission of the *Journal of Applied Physiology*

DEADSPACES, RESPIRATORY PATTERN AND RESPIRATORY RESPONSE TO CO_2

Table 1 contains data on deadspaces and arterial and alveolar P_{CO_2} and P_{O_2} gradients obtained from ten subjects from whom arterial samples were collected.

Table 1. Deadspace and Arterial–Alveolar PCO_2 and PO_2 Gradient in Chronic Respiratory Acidosis (10 Subjects)

Condition	Control	40 days exp. to 1.5% CO_2	9 day recovery on air	4 weeks recovery on air
Physiological deadspace (ml)	169	273*	262*	174
Physiological deadspace per cent Tidal Volume	29%	35%	37.6%	27%
Anatomical deadspace (ml)	157	214*	213*	163
Alveolar deadspace (ml)	12	59*	49*	10
Alveolar P_{CO_2} mm Hg	38.2	39.6*	39.9	37.4
Arterial P_{CO_2} mm Hg	39.4	44.9*	43.9*	38.3
Δ Arterial–Alveolar P_{CO_2} mm Hg	1.3	5.3*	3.8*	8
Δ Arterial–Alveolar P_{O_2} mm Hg	10.6	24.9*	20.3*	13.4

* Statistically Significant

Anatomical deadspace rose during CO_2 exposure from 28 per cent of tidal volume to 33–35 per cent which suggests a dilatory effect of CO_2 on the airways. Physiological deadspace, alveolar deadspace and $Pa-P_ACO_2$ gradient, as well as P_AO_2–PaO_2 gradients increased during exposure to CO_2. These findings indicate an increase in unperfused and unventilated alveoli during prolonged exposure to CO_2. Severinghaus and Stupfel (1957) and Severinghaus, Stupfel and Bradley (1957) have shown that the alveolar deadspace increases with increasing tidal volume and that the arterial-alveolar CO_2 gradient has a positive correlation with alveolar deadspace. It seems, therefore, that subjects who normally have a large tidal volume while breathing air and show a low response to CO_2 will have a certain degree of alveolar deadspace.

The increase of alveolar deadspace found during chronic exposure to 1.5 per cent produces a buffering effect on the gas composition of the alveoli. If a certain percentage of alveoli are well ventilated but poorly perfused, the gas composition of the alveoli will be altered towards that of the deadspace gas as outlined by Ross and Farhi (1960), leading to a reduction of the alveolar P_{CO_2} and an increased arterial alveolar P_{CO_2} gradient. A large alveolar deadspace will produce and maintain a higher arterial CO_2 tension and a correspondingly larger buffer capacity (bicarbonate) in the arterial blood. If CO_2 is inhaled under these conditions a mechanical buffering of CO_2 in the lungs is combined with a chemical buffering in the blood which will effectively reduce the development of peak CO_2 tensions in arterial and mixed venous blood and thereby limit the respiratory response to CO_2.

The lower response to CO_2, found in subjects with a larger tidal volume, is related to several factors. Besides an increased deadspace ventilation mechanical factors play a role. Evidence for the influence of the latter has recently been furnished by Milic-Emili and Tyler (1963) who demonstrated a linear relationship between alveolar CO_2 tension and the rate of mechanical work of inspiratory muscles. Moreover, the effort required by the inspiratory muscles to maintain a given level of pulmonary ventilation increases with increasing tidal volume because of the greater amount of elastic work involved (Otis, 1954). Since the rate of work is the same for the same deviation of P_ACO_2, it was concluded that an increased tidal volume would have to result in a reduction of the ventilatory response to CO_2 (Milic-Emili and Tyler, 1963).

Table 2. Ventilatory Response to 5 per cent CO_2 before, during and after Exposure to 1.5 per cent CO_2 over a Period of 42 Days, 21 Subjects

		1	2	3
		Test in submarine during control period on air	Test in submarine after 40 days exposure to 1.5 per cent CO_2	Test in laboratory 3 weeks after exposure to 1.5 per cent CO_2
Total group of subjects respir. min. vol.		l/min BTPS	l/min BTPS	l/min BTPS
	Mean	17.91	14.58*	18.91
	S.D.	3.68	2.46	3.88
	N	21	21	21
Low ventilation group respir. min. vol.	Mean	14.80	14.60	16.07
	S.D.	2.69	2.76	3.49
	N	7	7	7
High ventilation group respir. min. vol.	Mean	19.47	14.57*	20.33
	S.D.	3.04	2.31	3.22
	N	14	14	14

* Difference between results of Test No. 2 and Test No. 1 (control) statistically significant at the 1 per cent level and better

The ventilatory response to 5 per cent CO_2 measured after 35–41 days of exposure to 1.5 per cent CO_2 in 21 subjects is significantly depressed compared with control values prior to exposure and data obtained after four weeks recovery on air (Table 2). These results show a close parallelism to experiments after 3 per cent CO_2 exposure for three and six days, in which the same effect was observed (Haebisch, 1949; Schaefer, 1949). If the subjects are classified in a low and high ventilation group, according to the previously used procedure (Schaefer, 1958), it can be noted that the low ventilation group does tolerate the exposure to 1.5 per cent CO_2 without significant depression of the ventilatory response to 5 per cent CO_2 (Table 2). These subjects must be already partially adapted to a higher CO_2 level before they are exposed to 1.5 per cent CO_2 and should show a respiratory pattern found to be associated with (1) the lowered response to CO_2 in acute conditions, and (2) respiratory acclimatization to CO_2. Confirmatory evidence for this hypothesis is shown in Table 3.

Table 3. Respiratory Pattern of Low (A) and High (B) Ventilation Groups while Breathing Air Tested before, during and after Exposure to 1.5 per cent CO_2

	N	Test in submarine control period on air	Test in submarine, 40 days exposure to 1.5 per cent CO_2	Test in laboratory 4 weeks after exposure to 1.5 per cent CO_2
Group A: low ventilation group				
Respiratory rate	7	8.0 (2.3)	8.0 (2.0)	7.6 (1.4)
Tidal volume, ml (BTPS)	7	820 (260)	827 (290)	741 (170)
Group B: high ventilation group				
Respiratory rate	14	10.5* (2.1)	10.1 (3.4)	11.2* (3.0)
Tidal volume, ml (BTPS)	14	634 (190)	660 (220)	652 (260)

* Differences between two groups statistically significant at the 5 per cent level and better

HISTOPATHOLOGICAL STUDIES ON LUNGS OF ANIMALS IN CHRONIC HYPERCAPNIA

Histopathological studies on guinea pigs exposed to 1.5 per cent CO_2, 3 per cent CO_2 and 15 per cent CO_2 for prolonged periods showed the development of atelectasis and hyaline membrane formation in subpleural regions during exposure to 3 per cent CO_2 and 15 per cent CO_2. Incidence of both hyaline membranes and atelectasis decreased during the compensatory phase of CO_2 exposure, suggesting an adjustment of gas exchange and blood flow during this period (Niemoeller and Schaefer, 1962). Evidence for a direct effect of CO_2 on the mitochondria of alveolar lining cells, resulting in a decrease of surface active material, has recently been found in guinea pigs exposed to 15 per cent CO_2 (Schaefer, Avery and Bensch, 1964).

ACID BASE BALANCE AND ELECTROLYTE SHIFTS

In chronic respiratory acidosis induced by prolonged exposure to 1.5 per cent CO_2, some characteristic changes occur in electrolytes. Mention is made only of the cation exchange in the red cells, as an indication of CO_2 adaptation. The red cells showed an increase of sodium, after 35–41 days of exposure to CO_2 and during 8 to 9 days of recovery on air, that was associated with an approximately equivalent reduction of potassium in the red cells (Schaefer, 1964) (Table 4).

Table 4. Erythrocyte Cation and Anion Exchange in Chronic Respiratory Acidosis (10 Subjects)

Condition	Control	35–41 days exposure to 1.5 per cent CO_2	9 days recovery on air	4 weeks recovery on air
Na, mEq/L Red Cells	13.5	21.6*	24.4*	12.8
K, mEq/L Red Cells	86.0	78.9*	76.2*	79.9
HCO_3mMol/L Red Cells	14.3	17.0*	17.0*	16.3*
CL, mEq/L Red Cells	55.8	58.3	56.9	58.8

* Statistically significant

A similar shift of sodium into the red cells and an associated potassium loss was found clinically in cases of respiratory acidosis combined with decompensation and congestive heart failure (Buckley and Siecker, 1961).

ADAPTATION PROCESSES TO BREATH-HOLD DIVING

Since the skin diver is exposed to rather high CO_2 tensions and low O_2 tensions during the breath-hold dive (Schaefer and Carey, 1962) (Figs. 4, 5), one would expect to find an adaptation to high CO_2 and low O_2.

The ventilatory response to 10.5 per cent CO_2 was measured in a group of laboratory personnel serving as controls and instructors at the Espace Training Tank and found significantly reduced in the latter group. Moreover, the trained divers (instructors) showed a better oxygen utilization (low ventilation per liter oxygen uptake) and accepted a significantly larger debt during 33 min of exposure to 10.5 per cent O_2 than the group of laboratory personnel (Schaefer and Alvis, 1951).

The CO_2 tolerance curves were obtained by exposing subjects for 15 min to 3.3, 5.4, and 7.5 per cent CO_2. Alveolar ventilation and alveolar gas CO_2 tensions were determined at the end of each exposure period. The stimulus response curves (or tolerance curves) to CO_2 showed, in the case of the tank instructors, a shift to the right and a decreased slope (Schaefer, 1955 and Schaefer *et al.*, 1952). The high tolerance to CO_2 is developed during the diving period and lost after a three-month layoff

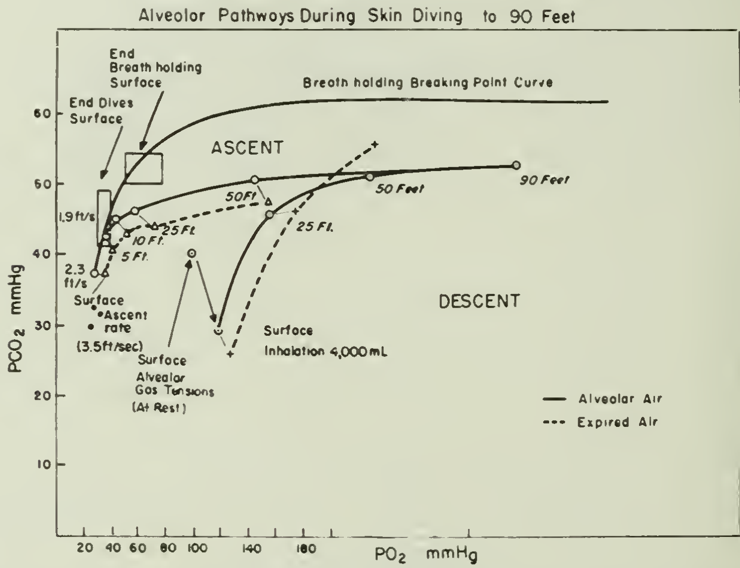

FIG. 4. Alveolar pathways during breath-holding dives to 90 ft showing reversed CO_2 gradient. At 50 ft P_{CO_2} mixed expired air is 6 mm Hg higher than P_{CO_2} "alveolar air." Surface breath-holding breaking point curve drawn for comparison with diving breath-holding curve. End dive alveolar P_{CO_2} decreased with increasing rate of ascent reaching 30 mm Hg at 3.5 ft/sec. Printed with permission of *Science*

period as shown in CO_2 sensitivity tests in eight tank instructors (Schaefer, 1961). Blood gas and electrolyte changes observed at the end of a longer period of water work were similar to those noted during adaptation to prolonged exposure to CO_2 (Schaefer, 1963). They consisted in a decrease in pH, increase in P_{CO_2} and bicarbonate levels commensurate with an increase in hematocrit and a red cell cation exchange, e.g. increase in red cell sodium and decrease in red cell potassium. These adaptive changes disappeared after a 3-month layoff period (Schaefer, 1961). Evidence of an increase in CO_2 stores, as the result of diving, was recently obtained in instructors following a two-year period of water work when compared with data obtained after a 3-month layoff period (Dougherty and Schaefer, 1962). During constant hyperventilation, lasting for one hour, more CO_2 was eliminated and the end tidal CO_2 tension was significantly elevated under the first condition. The decreased sensitivity to CO_2 and low O_2 found in skin divers represents an adaptation similar to that observed in diving animals (Irving, 1939).

The lung volumes of divers were also found to change during prolonged training (Carey, Schaefer and Alvis, 1956). A longitudinal study was carried out and the lung volumes of tank instructors measured at the beginning of their tour of duty and after one year. Inspiratory reserve, tidal volume, vital capacity, and total

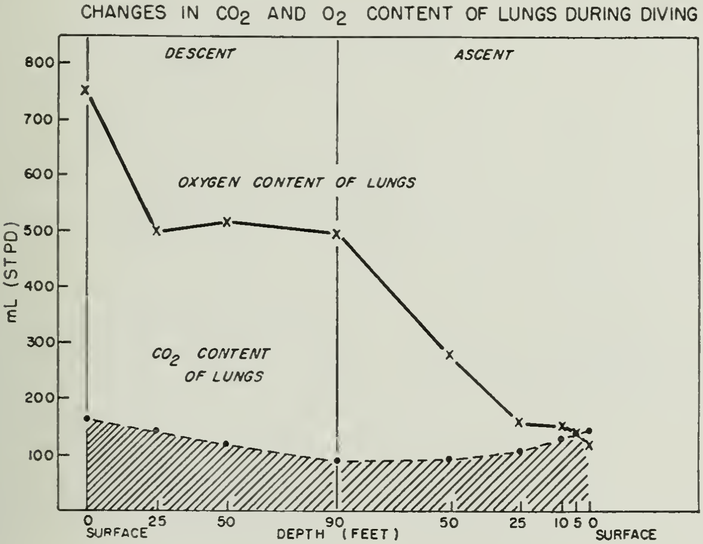

FIG. 5. CO_2 and O_2 content of lungs during diving (milliliters, STPD) calculated from measured gas tensions and volumes of mixed expired and alveolar air at various depths, the known residual volume and the total dry gas pressure in the lungs. Printed with permission of *Science*

capacity showed a significant increase while residual capacity decreased. The maximum average depth a diver can reach without getting a thoracic squeeze depends on the ratio of total lung capacity to residual capacity and the volume of the airways. The observed change in his ratio results in a 20–30 ft extension in the maximum safe depth after one year of duty. The changes in lung volumes, consisting of an increase in total lung capacity, vital capacity and tidal volume, and decrease in residual volume, might contribute to the reduced sensitivity to CO_2 because of the relationship found between large tidal volume, slow respiratory rate and low response to CO_2 (Schaefer, 1958).

ADAPTATION TO SCUBA AND DEEP SEA DIVING

Scuba Diving

Using open or closed circuit Self Contained Under Water Breathing Apparatus (SCUBA) units at a greater depth, the direct effect of pressure produces an increased density of the breathing mixture resulting in an increased breathing resistance. Under these conditions, the work of breathing was found decreased in both breathing apparatus and in the airways of the diver (Mead, 1955, Marshall, Lanphier and DuBois, 1956). Pulmonary resistance at 4 atmospheres pressure increased twofold compared with the values at sea level (Mead, 1956). Froeb (1961) compared the respiratory response to CO_2 in 16 professional divers using SCUBA equipment with those of non-divers and did not find any evidence of adaptation to CO_2 in the SCUBA divers. In studies of well trained underwater swimmers of the U.S. Navy Underwater Demolition Team (UDT) and untrained swimmers (laboratory personnel), using a closed circuit oxygen breathing apparatus, a higher mean end tidal P_{CO_2} tension was found in the trained swimmers during dives at a speed of 1.1 to 1.8 km/hr (Goff, 1957). For resting conditions underwater, differences were insignificant. The end tidal P_{CO_2} values of the trained swimmers ranged from 46.2 to 52.1 mm Hg as compared with 37.4 to 38.5 mm Hg in the control group. The higher end tidal P_{CO_2} values of the UDT men were found to be associated with a better oxygen utilization as indicated in the lower oxygen equivalent of 19.1 to 20 liters ventilation per liter of O_2 uptake compared with 21.3 to 24.6 in the controls. The trained swimmers showed a characteristic breathing pattern of slow deep breaths with long post-inspiratory pauses. They also had a larger tidal volume than the control group. These findings indicate a measure of CO_2 adaptation similar to that found in skin divers reported above.

Furthermore, adaptation to an increased work of the inspiratory muscles might have contributed to the elevated P_{CO_2} in the trained underwater swimmers because it was shown that the alveolar P_{CO_2} increases linearly with the workload of the inspiratory muscles (Milic-Emili and Tyler, 1963).

Deep Sea Diving

In deep sea diving ("Hard Hat Diving"), in which the conventional suit and helmet are used, a large amount of air has to be ventilated to prevent an accumulation of CO_2. Often this may not be fully accomplished. Moreover, at greater depths, breathing resistance becomes very marked and might easily lead to CO_2 retention. Lanphier found that a considerable number of experienced deep sea divers at the U.S.N. Experimental Diving Unit showed a retention of CO_2 during underwater work (1955a, b). The respiratory minute volume declined during work dives to moderate depth using oxygen-nitrogen mixtures. The degree of retention of carbon dioxide was found to be related to the ventilatory response to CO_2 (Lanphier, 1956). When breathing resistance was reduced by the use of helium-oxygen mixtures, the CO_2 retention was small or absent.

A more detailed account of adaptation in diving has been given elsewhere (Schaefer, 1965).

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INTERACTION OF INERT GASES WITH MOLECULAR CELL PROCESSES

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Abstract – Sufficiently high concentrations of He, Ne, Ar, Kr, and Xe and other inert gases reduce the responses of intact organisms to stimuli, and affect cellular metabolism, development, and radioresistance. While these physiological responses must be based on some form of molecular interaction, inert gases are incapable of interacting with each other or with the molecular environment of the living cell with chemical forces. However, metabolically inert gas molecules can draw upon long-range intermolecular forces of electromagnetic origin to produce weak interactions which set in motion apparently complex trains of physiological alterations leading to overt and significant biological manifestations such as xenon anesthesia. The basic molecular parameter that governs in a quantitative manner the strength of these interactions is the polarizability of inert gas molecules. This physical property can be regarded as a measure of the ease with which electrons can be displaced from their normal molecular charge distribution. Since the intensities of long-range intermolecular interactions vary inversely as high powers of the distance of intermolecular separation, steric relationships and intermolecular proximity within the cell must have an important qualitative and quantitative bearing on the observed biological effect. Nevertheless reasonably good correlations can be drawn between the polarizability of inert gases and the degree of their biological effectiveness. Indeed, all theories proposed to date to account for the biological manifestations of metabolically inert gases can be reduced to the consideration of molecular polarizability.

Zusammenfassung – Ausreichend hohe Konzentrationen an He, Ne, Ar, Kr, Xe und anderen inerten Gasen vermindern die Reaktion des Organismus auf Reize, beeinflussen den Zellstoffwechsel, die Entwicklung und die Strahlenresistenz. Diese physiologischen Reaktionen müssen auf einer Art von Molekülwechselwirkung beruhen. Inerte Gase können nicht untereinander wirken oder mit Molekülen in der lebenden Zelle über chemische Kräfte. Im Stoffwechsel unwirksame Gasmoleküle können jedoch auf intermolekulare Kräfte elektromagnetischen Ursprungs wirken, indem sie schwache Wechselwirkungen erzeugen, die offensichtlich komplexe physiologische Reaktionen auslösen. Diese führten zu deutlichen biologischen Wirkungen, wie sie in der Xenon-Narkose vorliegen.

Résumé – Des concentrations suffisantes en He, Ne, Ar, Kr, Xe et autres gaz rares diminuent la réaction de l'organisme aux irritations, influencent le métabolisme, le développement et la résistance au rayonnement. Ces réactions physiologiques doivent nécessairement reposer sur une interaction moléculaire. En effet, ces gaz rares ne peuvent ni agir entre eux ni réagir chimiquement avec des molécules des cellules vivantes. Les molécules gazeuses, inactives dans le métabolisme, peuvent pourtant se faire sentir par des forces intermoléculaires d'origine électro-magnétique en provoquant de faibles interactions qui déclenchent manifestement des réactions physiologiques complexes. Ceci conduit à des effets biologiques notables semblables à ceux observés dans la narcose au Xénon.

While anatomical, physiological and biochemical circumstances determine the concentrations of oxygen and carbon dioxide in living cells, the concentration of metabolically inert gases tends to reach equilibrium levels which depend solely on the external gas pressure, temperature, and on the chemical composition of the intracellular environment. As long as these parameters remain unchanged, a cellular system exposed to air will contain constant amounts of the metabolically inert constituents of air, i.e. nitrogen and the gases of the helium group. Against this background of constancy it is not surprising that the biological significance of these gases became appreciated only as man experienced exposures to artificial atmospheres containing these metabolically inert gases at increased partial pressures.

During the course of the next few minutes I shall briefly review the biological effects of these gases and attempt to relate them to molecular interactions that occur on the cellular and subcellular level. Metabolically inert gases are apparently non-essential to life (Barach, 1934; MacHattie and Rahn, 1960). At sufficiently high concentrations they can reduce the responses of intact organisms to stimuli, produce narcosis and affect cellular metabolism, development, and radioresistance (Rinfret and Doebbler, 1961; Featherstone and Muehlbaecher, 1963). Nitrogen is probably, although not necessarily (Volskii, 1959; Boriskin *et al.*, 1962; Allen, 1962) metabolically inert in higher forms of life but it is readily metabolized by a number of microorganism species. Of the gases of the earth's atmosphere, therefore, only helium, neon, argon, krypton and xenon are metabolically inert without qualification.

Probably the most striking biological effect of these gases is the anesthesia produced in man by the inhalation of an 80–20 mixture of xenon and oxygen at 1 atm pressure. Postulated and demonstrated in animals by Lazarev (1941, 1948) and Lawrence *et al.* (1946) this effect has been studied extensively in man during the past decade by Cullen, Pittinger and Gross and their associates (Cullen and Gross, 1951; Cullen and Pittinger, 1952; Pittinger *et al.*, 1952; Pittinger *et al.*, 1953; Morris *et al.*, 1955) who have shown that xenon possesses sufficient narcotic potency to provide surgically useful anesthesia.

These findings have sparked a new interest not only in the mechanism of anesthetic action (Cullen *et al.*, 1962) but also in the physiological properties of metabolically inert gases in general.

Several authors, notably Cook and South, have observed a number of biological effects of these gases both on the organism and the cellular level. Helium, and to a lesser extent argon, were reported to accelerate metamorphosis in the fruit fly, *Drosophila melanogaster*, and the meal worm *Tenebrio molitor* (Cook, 1950). Frankel and Schneiderman (1958) were unable to corroborate the findings made with *Tenebrio*, but were able to demonstrate that under atmospheric pressure another chemically unreactive gas, sulfur hexafluoride, inhibited adult emergence of the chalcid wasp, *Mormoniella vitripennis.* This insect was also shown to be subject to inert-gas narcosis at 10 atm pressure, with argon producing a moderate, and nitrogen a slight narcosis; helium had no effect at all. Nitrogen and argon inhibited the development of *Mormoniella* at 5 atm pressure.

A significant acceleration of the oxygen consumption of mice breathing an 80–20 $He-O_2$ mixture was observed by Young and Cook (1953), who concluded that the effect of helium is inversely proportional to the level of the animal's standard metabolism. The same gas mixture was shown to accelerate the *in vitro* oxygen consumption by striated muscle, liver, brain and sarcoma tissue of the mouse (Cook *et al.*, 1951; South and Cook, 1953). Helium was also reported to depress the rate of anaerobic glycolysis in mouse brain, liver and diaphragm tissue (South and Cook, 1953; Cook and South, 1953). These authors postulated that the glycolytic cycle is the site of both an inhibitory and an acceleratory effect of helium. The locus of the inhibition appears to lie above the aldolase reaction and that of the acceleration between the aldolase and the enolase reactions (South and Cook, 1953). Later Leon and Cook (1960) pointed out that the accelerated metabolism of rats exposed to a helium-oxygen environment is due to the greater heat loss in the presence of helium and that the magnitude of this response is proportional to the thermal gradient between the animal and its environment. However, since heat production is not regulated by isolated tissues but is a function of the intact organism, the observed cellular effect of helium must have a different explanation (Cook and Leon, 1959).

Several investigators have examined the effect of helium group gases at pressures above 1 atm. The earlier studies in this field have been motivated by a concern for the safety of divers, as exemplified by the work of Behnke and his collaborators (Behnke and Yarbrough, 1938, 1939). The lower solubility of helium in blood and other tissues relative to nitrogen provides a certain advantage in reducing the time required for decompression of divers and caisson workers (Gersh *et al.*, 1945). The narcotic action of helium is negligible at the pressures ordinarily encountered in such work; while nitrogen, as well as argon, produces definite narcotic effects in man under certain diving conditions.

Carpenter (1953), who studied the physiological effects of inert gases under pressure, reported that the following pressures (atm) were needed to protect 50 per cent of a given mouse population from convulsive seizures following supramaximal electric shock: N 24.8, Ar 12.6, sulfur hexafluoride 1.9, and nitrous oxide 0.6. He related (Carpenter, 1954) these observations to the facility of these gases to dissolve in olive oil or other non-polar liquids to produce a critical concentration of gas molecules at the site of their cellular action. At blockade pressure (12 atm) of isolated rat sciatic nerve conduction, xenon caused a drastic inhibition in the resting respiration of the nerve (Carpenter, 1956). Ferguson and Hawkins reported on the toxic action of several inert gases at high pressure on the grain weevil *(Sitophilus granarius)*; exposing the insects for 5 hr at 25° C in the presence of 1 atm. air, the following LD 50 pressures (atm) were noted: N 340, Ar 92, and nitrous oxide 14.5. The biological effectiveness of these gases followed the same order as was later seen by Carpenter.

Xenon under a pressure of less than 17 atm has been shown by Sears and Gittleson (1961) to inhibit the movement of single celled organisms of the genus *Paramecia*. This narcotic effect, produced in the absence of synapses, was not observed under 68 atm of either Ar, HE or N.

Table 1. "Inert" Gas Effect on the Growth of Neurospora Crassa 5297a

"Inert" gas	Molecular weight	Number of observations	Average lag phase (hr)	Average growth rate (mm/hr)
He	4.0	5	11	·3.51
Ne	20.2	6	12	3.14
Ar	39.9	10	13	2.73
Kr	83.8	11	13	2.22
Xe	131.3	12	12	1.86
N_2	28.0	12	9	2.93

$t = 30°$ C; "Inert" gas concentration: 0.95 atm

In our own laboratory we have studied the responses of a relatively simple biological system, the bread mold *Neurospora crassa*, to synthetic atmospheres containing one or more of the helium group gases (Schreiner *et al.*, 1962; Schreiner, 1963). As illustrated in Table 1, these gases affect in a systematic manner an important biological parameter, namely the cellular growth rate of this filamentous fungus. A plot of these data against the square root of molecular weight of the inert gases used results in the straight-line relationship shown in Fig. 1. Molecular weight,

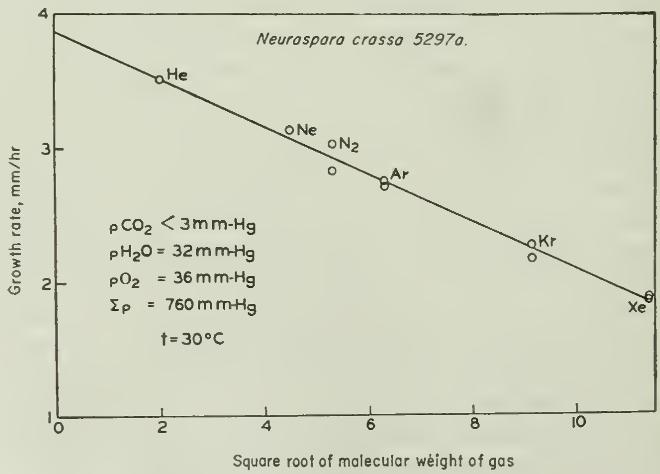

FIG. 1.

however, is not the critical gas property that manifests itself in these experiments. Sulfur hexafluoride, for example, is a metabolically inert gas of molecular weight 146.1 (vs. 131.3 for Xe), yet its effect on the growth rate of the experimental mold is no different than that of nitrogen. Nitrous oxide, on the other hand, with a molecular weight of 44, has a very pronounced inhibitory effect on the growth of this mold (Schreiner and Gregoire, 1963).

Since it is evident that most of the physiological responses to metabolically inert gases must be based on some form of molecular interaction, it is appropriate to recall that in the living cell, metabolically inert gases are incapable of interacting with each other or with their molecular environment with chemical forces. Thus, of the major types of molecular bonding shown below that are of significance in biological systems:

Type of Bond	Bond Strength in kcal
Covalent	40–140
Ionic	5
Hydrogen	2–5
van der Waals	0.5

chemically unreactive gases cannot form the first three of these bond types, which are conveniently, although somewhat arbitrarily grouped together as "chemical" bonds. So-called 'physical' or van der Waals bonding is a manifestation of long-range forces of electromagnetic origin that exist between molecules (Hirschfelder *et al.*, 1954). By way of contrast, short-range forces, frequently called valence or chemical forces, act between molecules that come close enough together for their electron clouds to overlap. In biological systems metabolically inert gases can manifest their presence only by way of long-range intermolecular forces that result from electrostatic induction and dispersion interactions between molecules. While these interactions are very weak, they appear to set in motion a complex train of physiological alterations that can produce observable effects. An understanding of the nature of these interactions is therefore essential to the assessment of the biological significance of metabolically inert gases.

Electrostatic long-range forces result from interactions between molecules possessing electric charges or dipole moments. Induction of a dipole in a non-polar molecule by the charge, or dipole of another, interacting molecule gives rise to intermolecular induction forces. In addition, two non-polar molecules may mutually induce dipoles in each other and thus interact. For the molecular interpretation of the biological effects of non-polar, chemically inert gases, induction and dispersion are the significant modes of interaction. Electrostatic interactions become important only with metabolically inert gases such as nitrous oxide that are permanent dipoles.

The force of interaction F between two spherical non-polar molecules is a function of the intermolecular separation r. The potential of interaction between these two molecules is the integral of this force over the distance in excess of r:

$$F(r) = -\frac{d\varphi}{dr} \quad \varphi(r) = \int_r^\infty F(r)\,dr$$

For non-polar molecules a commonly used intermolecular potential energy function is the Lennard–Jones (6–12) potential,

$$\varphi(r) = 4\,E\left[\left(\frac{\sigma}{r}\right)^{12} - \frac{\sigma}{r}^{6}\right]$$

where σ with the dimensions of length and E with the dimension of energy are constants that are characteristic of the chemical species of the interacting molecules. At large separations ($r \gg \sigma$) the inverse sixth power attractive component is dominant:

$$\varphi(r) = -4\,\varepsilon\left(\frac{\sigma}{r}\right)^6 - \frac{d\varphi}{dr} = -\frac{24\,\varepsilon}{r}\left(\frac{\sigma}{r}\right)^6$$

thus the molecules are attracted to one another with a force proportional to the inverse seventh power of the separation. This type of force describes accurately the induced dipole-induced dipole interaction between two non-polar molecules. This interaction occurs between two non-polar molecules a and b because at any instant the electrons in molecule a are in some configuration which results in an instantaneous dipole moment. This instantaneous dipole moment induces a dipole in molecule b. The induced dipole in b then interacts with the instantaneous dipole in a to produce an energy of attraction between the two molecules. This dispersion energy is described by the London equation,

$$\varphi_{ab}^{\mathrm{dis}} = -\frac{3}{4}\left(\frac{hv_a hv_b}{hv_a + hv_b}\right)\frac{\alpha_a \alpha_b}{r^b}$$

where hv_a and hv_b are characteristic energies of the two molecules approximately equal to their ionization potential; α_a and α_b are their polarizabilities.

Intermolecular induction energies are given by the relationships,

$$\varphi_{ab}^{(C,\,\mathrm{ind}\,\mu)} = -\frac{C_a^2 \alpha b}{2r^4}$$

where the charge C on molecule a has induced a dipole in molecule b of polarizability α_b, and

$$\varphi_{ab}^{(\mu,\,\mathrm{ind}\,\mu)} = -\frac{\mu_a^2\,\alpha b}{r^b}$$

where the dipole μ_a of molecule a has induced a dipole in molecule b of polarizability α_b.

These considerations make it evident that polarizability is the single most important physical parameter that governs the strength of long-range intermolecular forces.

Polarizability, which is a characteristic molecular property, can be regarded as a measure of the ease with which electrons can be shifted from their normal molecular charge distribution about one or more nuclei. Polarizability α is defined as follows:

$$m = \alpha F$$

where m is the electrical moment of the dipole induced by a field of strength F acting on a molecule. Polarizability may be determined from the molecular refraction $[R]$ by the following relationship:

$$[R] = \left[\frac{4\pi N}{3}\right]\alpha = \frac{n^2-1}{n^2+2}\cdot\frac{M}{d}; \quad \alpha = \frac{[R]}{2.52\times 10^{24}}$$

where N = Avogadro's number, n = index of reaction, M = molecular weight and d = density.

The biological significance of molecular polarizability manifests itself in many ways, as for example in the correlation, first pointed out by Wulf and Featherstone (1957), that exists between the potency of gaseous anesthetics and their polarizability. Since polarizability governs such intermolecular relationships as solubilities or distribution coefficients of gases in cellular materials, the classic Meyer–Overton theory of narcosis is but another expression of this basic molecular parameter.

Another important point that must be kept in mind when the forces of long-range molecular interactions are considered is that these forces vary inversely as high powers of the intermolecular separation. Steric relationships and, more generally, intermolecular proximity within the cell must therefore be given due consideration in the mechanisms that have been proposed to explain the biological effects of metabolically inert gases.

The views of Pauling (1961) and Miller (1961) concerning the association of water molecules with metabolically inert gases in living systems so as to interfere with normal cellular processes are recent attempts to offer such an explanation. While classical gas hydrates as they have been known to chemists for over 150 years (Schroeder, 1926) are probably not present as such under most circumstances that involve the exposure of biological systems to metabolically inert gases, measurable interactions of these gases with water molecules can be expected on the basis of what has been said so far.

However, we feel that yet another mechanism, equally based on interactions that are determined by molecular polarizability, deserves further exploration.

Among the more recent discoveries in the field of inert gas physiology, one observation is of special significance and merits a more detailed discussion at this time. In 1958, Ebert, Hornsey, and Howard (1958) demonstrated that inert gases can prevent the damage that ordinarily occurs when oxygen is present during ionizing irradiation. The meristem of the main root of the broad bean seedling *(Vicia faba)*, like many other tissues, is two to three times more sensitive to X-rays in the presence of oxygen than in its absence. Using as a measure of radiosensitivity the reduction of growth rate of the root (which is believed to be due predominantly to death of cells following chromosome damage), these authors discovered that normally unreactive gases have a radioprotective effect in living cells. The partial pressures of inert gases required when added to 1 atm of air to reduce the oxygen-dependent radiosensitivity of *Vicia faba* roots by one-half are shown in Table 2.

Table 2. Radioprotective Effect of Metabolically Inert Gases

Gas	Pressure in atm for 50 per cent effect	Solubility in oil (1 atm) cm^3 gas STP per 1000 g oil	Partition coefficient lipid–water
Helium	55	15 (37° C)	1.7 (37° C)
Hydrogen	55	50 (40° C)	2.3 (22° C)
Nitrogen	12.5	67 (37° C)	3.5 (22° C)
Argon	2	140 (37° C)	4.0 (22° C)
Krypton	2	430 (37° C)	7.5 (22° C)
Xenon	1.1	1700 (37° C)	14.5 (22° C)

Pressures of metabolically inert gases added to 1 atm of air to reduce the oxygen-dependent radiosensitivity of *Vicia faba* roots by one-half. (M. Ebert, S. Hornsey and A. Howard, 1958)

Similar radioprotective effects were found with Ehrlich ascites tumor cells and *Shigella flexneri*. These observations led to the postulation that "specific and finite sites exist within the cell at which oxygen must be present to confer oxygen-dependent radiosentivity, and that inert gases can displace oxygen from these sites." The parallel between effectiveness of a given gas and its lipid–water partition coefficient suggested to Ebert and his colleagues that the site of the adsorption displacement of oxygen may be associated with some lipid-like material in the cell. The unchanged rate of oxygen utilization in their experiments makes it unlikely that the site is one of the main cytosplasmic organelles which utilize oxygen. They conclude, "... the site of action of inert gases may be a lipid–water interface or an area of volume in the lipid fraction of the cell. Since the type of radiation damage which we have been measuring is expressed in the nucleus, and is believed to be the result of energy absorbed there, the site may well be within the nucleus or associated with the nuclear membrane."

The application of Ebert's conclusions to the observations made with *Neurospora crassa* — a system that shows an oxygen dependence of growth that parallels the oxygen dependence of radiosensitivity – leads to the postulation of states of "subcellular hypoxia" created by the displacement of oxygen from certain subcellular sites for which metabolically inert gases have a high degree of affinity. Additional experimental evidence for such a hypoxid mechanism of the biological effects produced by metabolically inert gases has come from the recent work of Bennett (1963).

Specific interactions of metabolically inert gases with protein molecules have been described by Featherstone and co-workers (1961). There is no reason to believe that similar specific interactions do not occur with other molecular structures of the living cell. The occupation by inert gases of subcellular sites associated with oxidative metabolic activity and the concommittant restrained access of molecular oxygen to these sites may be thought of as only one manifestation of molecular polarizability. On this basis we can expect other molecular processes such as membrane transport, enzyme reactions and even cellular replication to be subject to the action of metabolically inert gases.

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ADAPTATION TO DECOMPRESSION SICKNESS IN CAISSON WORK

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Abstract – Evidence is presented that acclimatization to decompression sickness occurs in the first ten days of exposure to compressed air. It is a temporary effect which is rapidly lost on ceasing to work in compressed air. At present, due to inadequate knowledge of the mechanisms concerned, there is no means of avoiding the acclimatization period.

Zusammenfassung – Es wird gezeigt, dass die Akklimatisation an Dekompressionserkrankungen während der ersten 10 Tage im Überdruck stattfindet. Es handelt sich dabei um eine vorübergehende Erscheinung, die nach Beendigung der Arbeit unter hohem Druck schnell verloren geht. Infolge unzulänglicher Kenntnisse über die beteiligten Mechanismen besteht gegenwärtig keine Möglichkeit die Akklimatisierungsperiode zu vermeiden.

Résumé – On démontre que l'acclimatation aux maladies de décompression se produit au cours des 10 premiers jours d'exposition à l'air comprimé. C'est un effet seulement temporaire qui se perd rapidement dès que l'individu ne travaille plus dans l'air comprimé. Par suite de connaissances insuffisantes des mécanismes mis en cause, il est encore impossible de supprimer la période d'acclimatation.

It HAS generally been thought that adaptation to decompression sickness does not occur and, in fact, that sensitivity may increase with continued exposures to compressed air. In 1954, Paton and I reported evidence that acclimatization to work in compressed air can occur.

During the construction of the first Tyne Tunnel, 1948–1950, we were able to study the 376 compressed air workers involved. Decompression was carried out at the very beginning in accordance with the table published in 1936 for the Institute of Civil Engineers of Great Britain, and then, as soon as it was available, by the table compiled by Damant and Paton for the Compressed Air Committee of the Institute of Civil Engineers and Ministry of Labour. Both these tables represent modifications of the Haldane two-stage procedure. Pressures up to 38 psi were experienced. In all, 40,000 compressions were carried out, and there were 350 cases of "bends" in 181 of the 376 men.

The weekly incidence of "bends" is illustrated in Fig. 1. It shows two features:

(1) A considerable week to week fluctuation in "bends" rate.

(2) A tendency for the "bends" rate to diminish as the work progressed. The calculated regression line of "bends" incidence on time is shown.

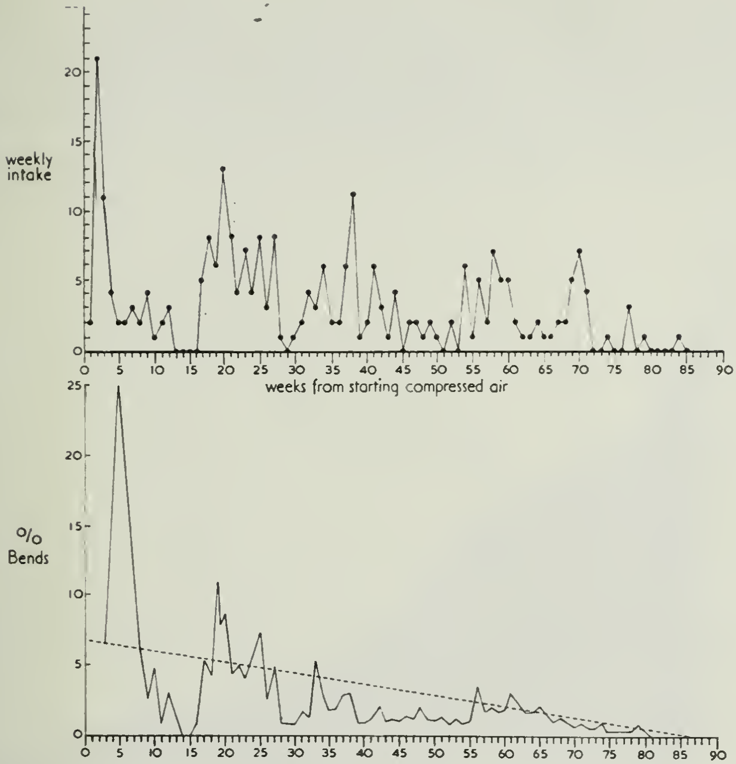

FIG. 1. Weekly incidence of "bends" and intake of new labour. Tyne Tunnel

FIG. 2. The relationship between "weekly" bends incidence and intake of new labour. Tyne Tunnel. ($r = 0.836$)

The marked weekly fluctuation was shown to coincide with the influx of new labour (Fig. 2) but the general tendency for the mean "bends" rate to fall from more than 6 per cent to almost zero could not be accounted for in this way. This general tendency to fall might be explained by acclimatization or by selection resulting from the elimination of susceptible individuals from the population at risk or by a combination of both these phenomena.

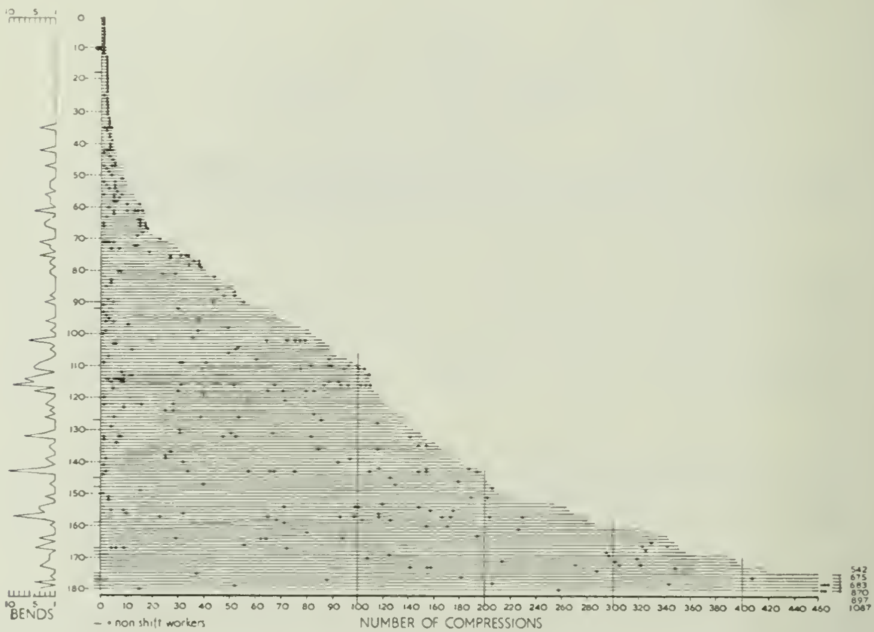

FIG. 3. "Bends" history of 181 compressed air workers. Tyne Tunnel.
• = attack of "bends"

If acclimatization is the explanation, then the "bends" incidence of a working force, the members of which all start working at the same time and to which there are no additions, should steadily fall from a fairly high initial value.

From our data, we selected all those men who had suffered "bends" at least once and adjusted their compressed air working histories so that they all appeared to start work on the same day. The resulting chart is shown in Fig. 3. The men are arranged in order of duration of employment and the time when each man suffered a "bend" is shown by a dot.

From this chart, it is possible to obtain the "bends" rate as a percentage for successive days of exposure for this particular population. The results are shown in Fig. 4 and appear to confirm the impression that susceptibility to decompression sickness declines with successive exposures.

There is, however, still the possibility that the decline in "bends" rate seen in Fig. 1 may be explained in part or in whole by the elimination of the susceptible members from the population. By examining groups of men from which none was shed over a period of time, the effect of the elimination of susceptibles was avoided.

Unfortunately, the use of this method results in the fact that large groups of workmen can only be followed for short periods of time (120 men, 10 compressions) whereas tests over long periods of time can only be applied to small groups of men (90 men, 50 compressions, and 80 men, 100 compressions).

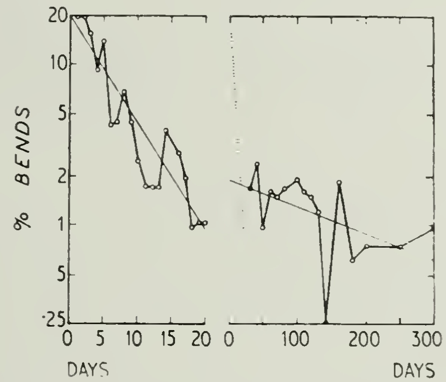

Fig. 4. Decline of "bends" incidence with time for workers shown in Fig. 3.
Tyne Tunnel
Left: 0 – 20 days with calculated regression line
$r = -0.976$
Right: 20 – 300 days with calculated regression line
$r = -0.4794$

Using this technique, acclimatization clearly appeared to be occurring. See Table 1 , (A), (B) and (C) and Figs. 5, 6 and 7.

When the rate of fall of "bends" incidence due to elimination of susceptible individuals was estimated for the men shown in Fig. 1, it was found to be about 1 per cent in every 150 days (Paton and Walder, 1954). A comparison between the rate of fall due to elimination of susceptibles and that due to acclimatization is shown in Fig. 8.

It is clear that whilst selection is occurring all the time, acclimatization accounts for the main fall in "bends" rate in the first 10 days.

At the Dartford Tunnel (Campbell *et al.*, 1960), we were able to observe a group of 22 steel erectors who had never been in air before, and who all started in compressed air on the same day.

They were followed for one month, during which time the tunnel pressure was constant. A plot of the number of "bends" against number of compressions is shown in Fig. 9. There is a large decline in "bends" incidence with the passage of

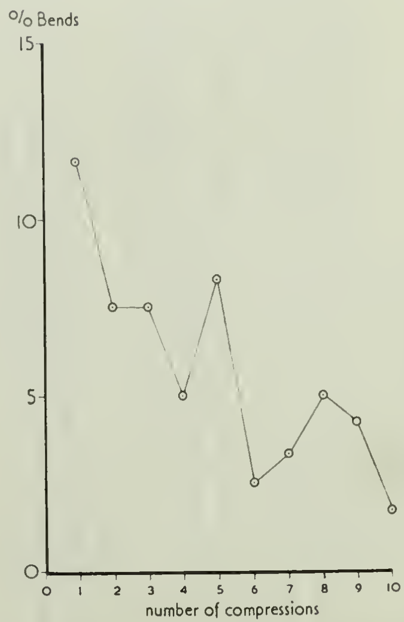

Fig. 5. Decline of "bends" incidence of 120 men for first 10 compressions

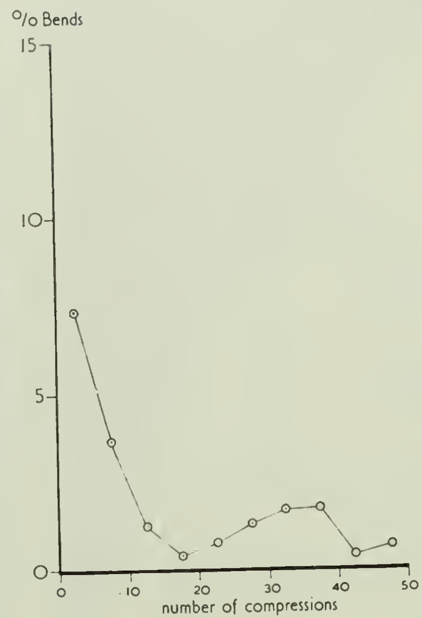

Fig. 6. Decline of "bends" incidence of 90 men for first 50 compressions

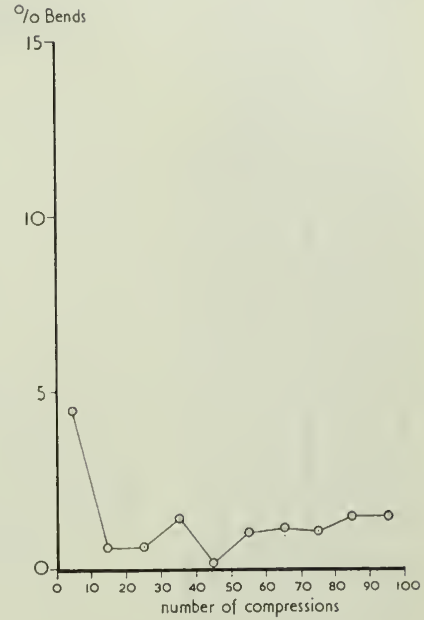

Fig. 7. Decline of "bends" incidence of 80 men for first 100 compressions

Table 1. The Effect on the Mean Daily Bends Rate of Repeated Daily Exposures to Work in Compressed Air

(A) 120 men, first 10 compressions

Compression no.	1	2	3	4	5	6	7	8	9	10
No. of bends	14	9	9	6	10	3	4	6	5	2
Bends %	11.7	7.5	7.5	5.0	8.3	2.5	3.3	5.0	4.2	1.7

(B) 90 men, first 50 compressions

Compression No.	1–5	6–10	11–15	16–20	21–25	26–30	31–35	36–40	41–45	46–50
No. of bends	33	16	6	2	4	6	8	8	2	3
Bends %	7.3	3.6	1.3	0.44	0.89	1.3	1.8	1.8	0.44	0. 67

(C) 80 men, first 100 compressions

Compression no.	1–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	81–90	91–100
No. of bends	36	5	5	11	1	8	9	8	12	12
Bends %	4.5	0.63	1.4	0.1	1.0	1.0	1.1	1.0	1.5	1.5

time. The data are well fitted ($r = 0.97$) by the regression line log. 10 (number of bends) = 1.16–0.42 (number of compressions). Half time = 7 ± 4 days. This effect can only have been due to acclimatization.

For how long does acclimatization persist after ceasing to work in compressed air? This was investigated by scrutinizing the air histories of a large number of men to see whether an attack of "bends" occurred on returning to work after a period of absence. Weekends gave a large number of two-day lapses in regular working, and holidays or strikes gave a large number of lapses of 10 days or more. A few figures were obtained for the intermediate periods. Figure 10 shows the "bends" percentage after various intervals away from work. Unfortunately, the only groups with sufficient numbers to permit statistical analysis are the lowest and the highest points, the difference between which is highly significant.

Substantiation for the concept of acclimatization and de-acclimatization has recently come from the report of Rose (1962). During the construction of Pier 2 of

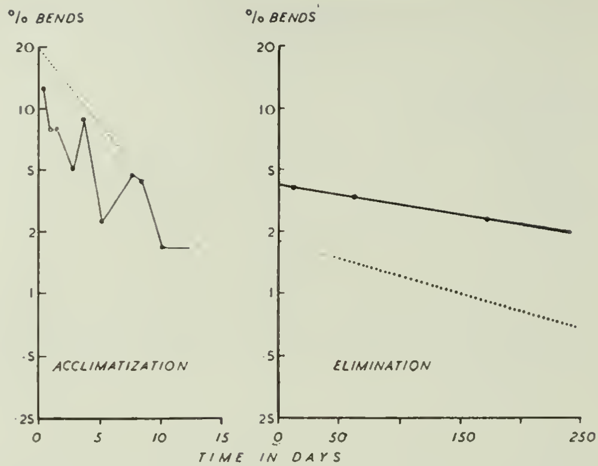

FIG. 8. Comparison between regression lines 0 – 20 days and 20 – 300 days for actual fall in "bends" incidence. Tyne Tunnel.

Left: Estimated rate of fall from acclimatization.

Right: Estimated rate of fall from elimination of susceptibles.

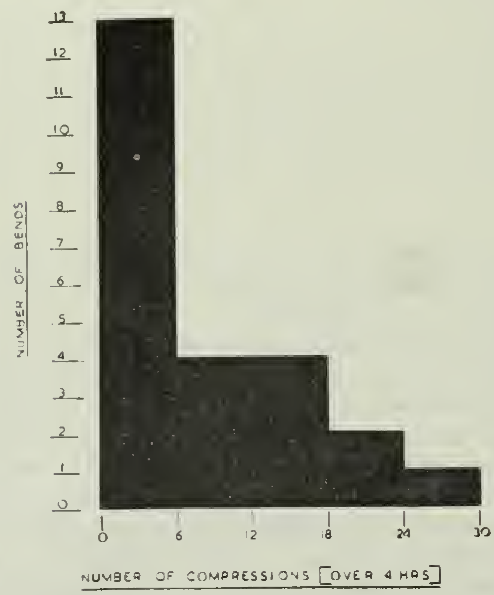

FIG. 9. Number of "bends" in steel workers following successive compressions Dartford Tunnel.

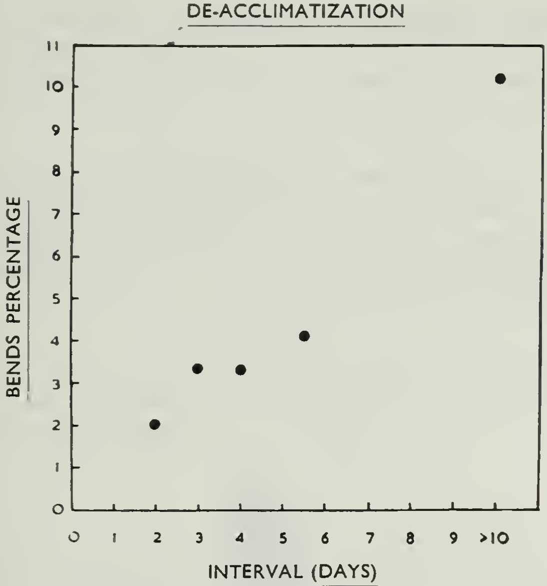

FIG. 10. Incidence of "bends" in groups of acclimatized men re-starting in compressed air after an interval away from work. Dartford Tunnel

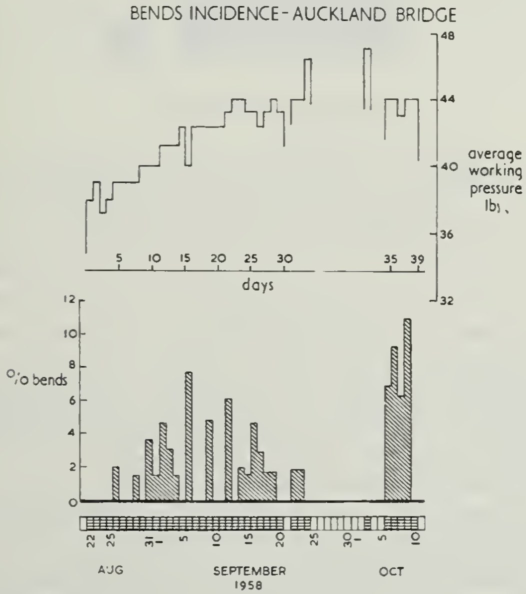

FIG. 11. Acclimatization and de-acclimatization in a group of men working in a Caisson for the Auckland Harbour Bridge

the Auckland Harbour Bridge, 69 shift workers underwent 1,823 compressions with 50 "bends" at pressures ranging between 37 and 47 psi. During this period there was clearly a phase of acclimatization once the pressure stabilized around 43 psi. This was followed by an 11-day strike, and a dramatic loss of acclimatization (Fig. 11).

The magnitude of the importance of acclimatization can best be demonstrated by supposing that if some scheme could be devised for introducing new starters and re-introducing those who had been off work to compressed air work safely, then in a 68-week period, the overall "bends" rate would be more than halved. The following methods have been suggested:

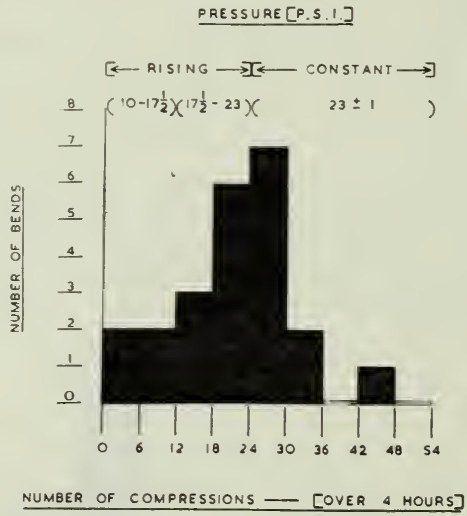

FIG. 12. "Bends" incidence during a period of rising pressure and during a period of steady pressure. Dartford Tunnel

(1) Working up to pressure over several shifts. Study at the Dartford Tunnel over a period when a progressive rise in pressure was occurring (Fig. 12) showed a progressive increase in the number of "bends" each day, but once a steady maximum level had been obtained, there was a fall in "bends" rate, presumably due to the acclimatization which then took place. There is then no value in working up to pressure over several shifts, as each rise in pressure leads to a fresh outbreak of "bends".

(2) Acclimatizing at a low pressure before exposure to a high pressure. Experience at the Dartford Tunnel suggests that no protection to the high pressure results from acclimatization to a low pressure.

(3) There remains the possibility of gradually increasing the duration of time worked at pressure, but since the half time for acclimatization is 7 ± 4 days, it is likely that such a technique would have to be prolonged.

POSSIBLE MECHANISM OF ACCLIMATIZATION

At the present time, it is only possible to speculate about the mechanism of acclimatization.

(1) Perhaps it can be compared with getting into training for athletics. Unaccustomed hard work may lead to muscle fibre rupture with consequent bubble nuclei formation. If this is so, then a period of surface work of a similar nature to that to be performed in compressed air might help.

(2) Perhaps individuals carry a stock of gas micronuclei in their tissues which become unstable and are used up at successive changes in pressure (Harvey, 1944).

(3) Perhaps the individual's sensory nerve endings are fatigued or are damaged so that successive distension of a bubble at one particular site eventually goes unappreciated.

CONCLUSIONS

Acclimatization occurs and is obviously of major importance. It is of short-lived duration once exposure to compressed air ceases.

"Bends" susceptible individuals should be reassured that perseverance with compressed air work will lead to an improvement in their resistance to "bends".

Some method of safely introducing men to compressed air work is required so that the acclimatization period of high "bends" frequency can be avoided.

ACKNOWLEDGEMENTS

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SUMMARY REPORT

K. E. SCHAEFER

The pioneer investigators in the field of high pressure environment, Captain Cousteau, and Captain Bond, submitted reports on recent experiments which gave a good account of the progress in this rapidly expanding area of research.

The paper of Cousteau and Alinat contains results of three experiments, with human subjects exposed to increased pressure under water; (1) two subjects lived submerged for seven days in compressed air at a depth of 10.5 m and performed working dives from this base to depths of 25 m (82 ft), (2) five subjects lived at a depth of 9 m in compressed air for one month, performing dives to a depth of 70 m (230 ft), (3) two men were exposed to helium–air mixture at a depth of 26.2 m for one week and made dives to 100 m.

Bond and co-workers carried out similar experiments in which three subjects lived for one–two weeks in a chamber, in the laboratory, while breathing helium–oxygen–nitrogen mixtures at: (1) normal atmospheric pressure, (2) 3.3 atm, 30.5 m depth, and (3) 7 atm, 61 m, depth.

In all these experiments subjects experienced no particular difficulties and basic physiological functions measured, such as weight, blood pressure, body temperature, and blood and urine chemistry, showed no significant alterations. However, in the first study reported by Cousteau's group, in which the partial pressure of oxygen in the atmosphere was twice normal (300 mm Hg), a marked decrease in total number of red cells associated with a fall in hematocrit was noted, indicating a depression of hematopoiesis. On the other hand, no changes in red cells and hematocrit were observed in Bond's experiment in which subjects lived under 7 atm with partial pressure of oxygen maintained at 205 mm Hg. These findings suggest that the threshold limit value of oxygen for continuous exposure lies between 200 and 300 mm Hg.

Schaefer reported about characteristic signs of adaptation to carbon dioxide (CO_2), such as increased tidal volume and lowered respiratory rate, lowered ventilatory response to CO_2 and a cation shift in the red cells (increase in sodium and decrease in potassium), which were also observed in skin divers. In Scuba and Deep Sea Divers, CO_2 retention was also noted. In the discussion, further aspects of adaptation to CO_2 were brought out, e.g. reduction of cerebral blood flow after an initial increase as shown by Betz in cats, using Hensel's thermal blood flow method.

Walder presented evidence of adaptation to decompression sickness based on the evaluation of a large number of observations on compressed air workers involved in the construction of the Tyne tunnel and the Dartford tunnel. It was possible to select subjects who worked consistently for longer periods, thereby avoiding the effect of the elimination of susceptibles to bends. In the discussion, the question was raised whether the workman compensation problem affected the rapid decline of incidence of bends during the first two weeks, e.g. it might have been desirable for a worker to establish, in the beginning of the work, that he had bends for purposes of later compensation. Walder felt that this factor did not play a role under the circumstances described.

Lanphier reviewed the effects of high pressure on respiratory mechanics. The increasing work of breathing is reflected in the decrease of Maximum Breathing Capacity (MBC), which is approximately halved at 4 atm and reduced to one quarter at 15 atm absolute while breathing air. The respiratory needs, for moderate exertion, can probably not be met with air at pressures much beyond four atmospheres abolute. These limitations of ventilation can be extended by the use of less dense gas, such as $He-O_2$ mixtures. However, these improvements do not seem to be of sufficient magnitude to allow exercise at extreme depth because of the reduced ventilatory capacity. The latter causes CO_2 retention, frequently observed in divers during exertion at higher pressures. This peculiar form of CO_2 retention in divers is not associated with symptoms of dyspnea, and is similar to the adaptation to CO_2 noted by Schaefer in submarine escape training personnel engaged routinely in breath-hold diving. Lanphier further discussed the role of CO_2 retention in oxygen toxicity producing a higher susceptibility to oxygen poisoning.

In the discussion the question was raised whether CO_2 retention is the cause of nitrogen narcosis, as previously advocated by Buehlmann. However, recent experiments of Lanphier demonstrated that nitrogen narcosis appears when there is no evidence of CO_2 retention.

Lenfant used the measurements of alveolar-arterial differences of P_{O_2} P_{CO_2} PN_2 to determinc the unevenness of the ventilation-perfusion ratio $\dot{V}_A/Q$ in the lungs under conditions of increased pressure. He showed that the uneven distribution factor can be determined by adding the A–a P_{N_2} and a–A P_{CO_2} differences. By subtracting the sum of the A–a P_{N_2} and CO_2 from the total A–a P_{O_2} the size of the anatomical shunt can be estimated. He found, in eight Navy divers exposed to 2.6 atm breathing 75 per cent oxygen, responses ranging from no change to a slight and significant impairment in ventilation-perfusion distribution and a small anatomical shunt. In the discussion of this paper, the importance of the measurements of A-a P_{N_2} differences was stressed as an important contribution to assess the changes in ventilation-perfusion ratios in the lung.

Schreiner presented a paper on the interactions of inert gases with molecular processes. In biological systems, metabolically inert gases cannot form chemical bonds, but can manifest themselves by way of long-range intermolecular forces that result from electrostatic, induction and dispersion interactions between molecules (van der Waals forces). The discovery of Ebert *et al.* that normally unreactive gases have a radioprotective effect, lead to the postulation that inert gases can displace oxygen from the sites within the cell at which oxygen must be present to confer oxygen dependent radiosensitivity. Furthermore, specific interactions of inert gases with protein have been described. All these findings indicate that the so called "inert" gases can have pronounced effects in living systems and also contribute to an understanding of nitrogen narcosis.

Nahas reported about the effects of daily injections of buffers, such as THAM and sodium bicarbonate, on oxygen toxicity in mice exposed to pure oxygen at one atmosphere during four weeks. THAM was ineffective, while sodium bicarbonate reduced the incidence of oxygen toxicity, but did not prevent degenerative testicular changes.

Bensch *et al.* reported about the time course of CO_2 effects on alveolar mitochondria and lung surface tension, showing that the transitory disappearance of lamellar bodies in the alveolar lining cells is correlated with an increase in lung surface tension. Both changes are confined to the uncompensated phase of respiratory acidosis.

A paper by Guillerm, Badré and Gautier was concerned with the effects of inhalation of 50 – 100 ppm of carbon monoxide and additional smoking on circulatory and respiratory reactions to exercise, as well as effects on night vision. Findings reported indicate an effect of smoking independent of the carbon monoxide hemoglobin level.

In summary, the papers presented during the workshop on high pressure environment and synthetic atmospheres demonstrated the significant advances made in this field during recent years. However, there are problem areas in which we still have a lack of knowledge, as was pointed out by the designated discussant Bohnenkamp. He emphasized that we still do not know whether man can live in an atmosphere completely devoid of nitrogen, although mice seem to be able to survive under these conditions for several weeks. More investigations are also needed to elucidate the gaseous exchange under conditions of higher pressure.

VETERINARY BIOMETEOROLOGY

Chairman: W. Bianca

CATECHOLAMINES, HYPOXIA AND THE METABOLIC RESPONSE TO COLD IN NEWBORN RABBITS

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Abstract – Experiments were conducted to test the hypothesis that the hypoxic depression of the metabolic response to cold in newborn rabbits is due to the inhibition by hypoxia of the calorigenic action of noradrenaline. It was found that in a cold hypoxic environment, the increase of the rate of oxygen consumption following noradrenaline (and other amines) was reduced, but not suppressed, when compared with the response in a neutral thermal environment in air. Thus, the role of catecholamines in the thermogenic response to cold and its depression by hypoxia is not a simple relationship.

Zusammenfassung – Es wird geprüft, ob die Hemmung des Stoffwechselanstiegs kälteexponierter neugeborener Kaninchen durch Sauerstoffmangel darauf zurückzuführen ist, dass die wärmebildende Aktion des Noradrenalins durch Sauerstoffmangel gehemmt wird. Es wurde festgestellt, dass in einer kalten, sauerstoffarmen Umgebung der durch Noradrenalin (und andere Amine) verursachte Anstieg des Sauerstoffverbrauchs verkleinert aber nicht aufgehoben ist. Diese Feststellung stüzte sich auf einen Vergleich mit Versuchen, die in einer thermoneutralen Umgebung und in Normalluft durchgeführt wurden. Hieraus geht hervor, dass die Rolle des Noradrenalins als wärmebildendes Agens in der Kälte sowie seine Hemmung durch Sauerstoffmangel, nicht eine Beziehung einfacher Natur darstellt.

Résumé – Des expériences furent conduites pour vérifier l'hypothèse que la dépression hypoxique de la réponse métabolique au froid chez les lapins nouveaux-nés est due à l'inhibition par la hypoxie de l'action calorigénique de la noradrénaline. On a trouvé que dans une ambiance froide et pauvre en oxygène, l'élévation du taux métabolique après absorption de noradrénaline (et autres amines) était réduite, mais pas éliminée, en comparaison avec la réponse dans une ambiance thermoneutre à l'air. Ainsi, le rôle des catécholamines dans la réponse thermogénique au froid et sa dépression par la hypoxie n'est pas une simple relation.

INTRODUCTION

The oxygen consumption of newborn animals, like that of adult ones, is increased at environmental temperatures below the thermoneutral zone conformable to their age (Dawes, 1961). This extra metabolism in the cold, however, is significantly reduced by hypoxia at all ages (Hill, 1959). Moore and Underwood (1960a, b) have suggested that noradrenaline may be a regulator of heat production in the cold in newborn animals. They found that the metabolic action of this catecholamine is suppressed by 10 per cent O_2 in a neutral thermal environment and proposed that the depression of the metabolic response to cold by hypoxia may be due to this hypoxic inhibition of the noradrenaline response (Moore and Underwood, 1960b). The present experiments were conducted to elucidate further the relation between this and other catecholamines and exposure to cold and to hypoxia on the oxygen consumption of newborn rabbits.

METHODS

The rate of oxygen consumption (by the closed-circuit technique of Scopes and Tizard, 1963) and the colonic temperature (by means of copperconstantan thermocouples) were measured in 14 unanesthetized rabbits, 1–7 days old (58–150 g), exposed to 35° C and 25° C, in air and in 10 per cent O_2 (in N_2). Noradrenaline, adrenaline, and isoprenaline, freshly prepared in acidified physiological saline, were administered intravenously in the standard dose of 2 μg/kg min (expressed in terms of the base), at the uniform rate of 0.015 ml/min for 10 min, in 2 or 3 matching infusions at 20-min intervals in each environment. The rabbits were not removed from the closed system for these infusions.

RESULTS

The results are summarized in Tables 1 and 2.

The Effects of Cold and Hypoxia

On exposure to cold (in air), the rate of oxygen consumption of these rabbits increased nearly twofold; concurrently, the colonic temperature fell, leveling off a mean 2° C below its initial value. Hypoxia, then, at once produced an abrupt and significant fall of the oxygen consumption to values near or below the minimal metabolic rate; the colonic temperature fell gradually a further 3° C during this time, without leveling off. Exposure to hypoxia in a neutral thermal environment did not significantly change the minimal rate of oxygen consumption; but colonic temperatures fell slightly in this environment.

The Effect of Noradrenaline

Fifty-five infusions of l-noradrenaline bitartrate were made in six rabbits 1–6 days old (weight: 87–127 g). In air, at 35° C, noradrenaline elicited promptly a mean twofold increase in the rate of oxygen consumption of these rabbits. The rise was steep, reaching its highest value in the last 2 min of the infusions. The decline of the oxygen consumption after the infusions was rapid at first, then more gradual, recovery being complete in 15 min. The colonic temperature increased a mean 1.2° C concomitantly with the rise in oxygen consumption during the infu-

Table 1. Mean and S.E. of the Rate of Oxygen Consumption of Newborn Rabbits Exposed to 35° C and 25° C, in Air and in 10 per cent O_2, Before and During Intravenous Infusions of Catecholamines, 2 μg/kg min for 10 min. The data are expressed as the average rise in the rate of oxygen consumption in ml/kg min, during the last 6 min of the infusions, compared with the last 10 min before the infusions

	35° C 21% O_2		35° C 10% O_2		25° C 21% O_2		25° C 10% O_2	
	Before	Infusion	Before	Infusion	Before	Infusion	Before	Infusion
Control	22.0 ± 1.6		19.3 ± 0.9		41.0 ± 3.6		26.8 ± 2.3	
Noradrenaline	22.9 ± 1.4	52.0 ± 2.3 +127%	20.2 ± 1.0	29.9 ± 1.9 +48%	43.2 ± 2.7	56.8 ± 4.1 +31%	25.8 ± 2.0	36.0 ± 2.5 +40%
Adrenaline	22.4 ± 1.7	29.6 ± 2.1 +32%	18.4 ± 0.5	26.4 ± 2.8 +43%	43.6 ± 5.8	44.9 ± 4.5 +3%	30.8 ± 3.9	31.2 ± 1.9 +1%
Isoprenaline	20.7 ± 1.8	40.4 ± 5.2 +95%	19.3 ± 1.4	29.4 ± 2.2 +52%	30.2 ± 2.3	40.0 ± 2.6 +32%	23.7 ± 1.0	29.8 ± 1.5 +26%

Table 2. Mean and S.E. of the Colonic Temperatures of Newborn Rabbits Exposed to 35° C and 25° C, in Air and in 10 per cent O_2 Before and During Intravenous Infusions of Catecholamines 2 μg/kg min for 10 min. The data are expressed as the average change in the temperature in °C during the last 6 min of the infusions compared with the last 10 min before the infusions

	35° C 21% O_2		35° C 10% O_2		25° C 21% O_2		25° C 10% O_2	
	Before	Infusion	Before	Infusion	Before	Infusion	Before	Infusion
Control	38.4 ±.07		38.1 ±.17		36.4 ±.53		33.1 ±.48	
Noradrenaline	38.5 ±.07	39.7 ±.66	38.3 ±.17	38.6 ±.30	36.4 ±.53	36.6 ±1.03	33.2 ±.46	33.3 ±.63
Adrenaline	38.8 ±.12	38.8 ±.16	38.6 ±.27	38.7 ±.48	36.9 ±.75	36.7 ±1.09	34.1 ±.75	34.3 ±.88
Isoprenaline	38.4 ±.14	39.3 ±.55	38.3 ±.12	38.7 ±.21	35.5 ±.66	35.6 ±.83	33.0 ±.46	33.2 ±.62

sions, but was slow declining afterwards. In the cold, the increase in the rate of oxygen consumption occurred more quickly and culminated earlier, but was significantly smaller than in thermoneutrality. However, the maximum rates of oxygen consumption induced by noradrenaline were not significantly different at 35° C and 25° C. The oxygen consumption reverted quickly toward control values after the infusions, recovery being complete in 10 min. The fall in the cold of the colonic temperature of these rabbits was halted or reversed during noradrenaline infusions; afterwards, it was resumed, but usually more slowly than before noradrenaline. Hypoxia significantly delayed the onset and reduced, but not abolished, the rise of the oxygen consumption during noradrenaline in the thermoneutral environment. The recovery time was correspondingly shorter. Colonic temperatures did not increase significantly during noradrenaline infusions under these conditions, and tended to fall after the infusions. Oxygen consumption during noradrenaline infusions in the cold also was significantly reduced, but not suppressed, by 10 per cent O_2. However, the increase in the rate of oxygen consumption was not significantly different from its pre-hypoxia control; it also was not different from the rise in thermoneutrality (in 10 per cent O_2). Recovery of the oxygen consumption after noradrenaline was usually delayed. Noradrenaline halted the rapid fall of the colonic temperature of these rabbits during cold in hypoxia. After the infusions, the temperatures fell more slowly than before or even rose.

The Effect of Adrenaline

Thirty-eight infusions of adrenaline bitartrate were given to 4 rabbits, 1–4 days old (58–99 g). In the thermoneutral environment, in air, adrenaline was significantly less effective than noradrenaline in increasing the rate of oxygen consumption of these rabbits. Hypoxia, however, had no significant effect on this response. In the cold, in air, adrenaline generally caused an abrupt significant fall of the oxygen consumption, followed by a gradual rise after the infusions, the O_2 consumption often attaining values higher than before adrenaline. Recovery proceeded very slowly and often was not significant, so that subsequent infusions were usually unsuccessful in further incrementing the rate of oxygen consumption. The action of adrenaline on the oxygen consumption in the cold was not significantly altered by 10 per cent O_2. Colonic temperatures were little affected by this catecholamine in all the environments.

The Effect of Isoprenaline

Thirty-six infusions of isoprenaline sulphate B.P., were administered to 4 rabbits, 4–7 days old (99–150 g). Oxygen consumption rose quickly during isoprenaline infusions at 35° C (in air), declining equally rapidly after the infusions. Under the conditions of these experiments, isoprenaline was intermediate between noradrenaline and adrenaline in the efficacy of inducing a significant increase in oxygen consumption. The colonic temperature rose a mean 0.9° C during the infusions, concurrently with the oxygen consumption, but was slower to fall afterwards. Hypoxia significantly depressed the increase of the rate of oxygen following isoprenaline at 35° C. Colonic temperatures increased correspondingly less and recovered more quickly in this environment. Infusions of isoprenaline during cold exposure in air produced significantly smaller increases in oxygen consumption than in the thermoneutral environment. Recovery of the oxygen consumption after isoprenaline was usually prolonged and incomplete. Hypoxia significantly reduced the metabolic action of isoprenaline in the cold and decreased the recovery time of the oxygen consumption after the infusions. The fall of the colonic temperatures in the cold, in air, was stopped or reversed by isoprenaline; but, in 10 per cent O_2, it was only slowed.

DISCUSSION

The large increase in O_2 consumption caused by the administration of noradrenaline suggested to Moore and others (1960a, b) that the metabolic response to cold in newborn animals might be regulated by this pressoramine. The depression by hypoxia of heat production in the cold might be due to the inhibition of this response to noradrenaline, according to these workers (1960b).

The present results confirm the observations of Scopes and Tizard (1963) that breathing 10 per cent O_2 does not suppress the rise in O_2 consumption produced by the intravenous infusion of noradrenaline in a thermoneutral environment, and extend these findings to isoprenaline, and to both noradrenaline and isoprenaline in a cold environment. The effect of these catecholamines on oxygen consumption was reduced but not abolished by hypoxia in newborn rabbits, contrary to the findings of Moore and Underwood (1960b). On the other hand, hypoxia (10 per cent O_2) always abolished in the present experiments the metabolic response to cold (25° C).

The findings with adrenaline support the conclusion of Dawes and Mestyán (1963) that its activity, while smaller than that of noradrenaline, is nonetheless significant. Furthermore, its effect on O_2 consumption was not affected by hypoxia.

Thus, it would appear that the role of the catecholamines in the metabolic response to cold and its depression by hypoxia is not a straightforward relationship.

SUMMARY

1. Experiments were conducted to elucidate the relation between catecholamines, hypoxia and the metabolic response to cold.
2. The metabolic action of intravenous infusions of noradrenaline and isoprenaline was reduced but not suppressed by 10 per cent O_2 in both thermo-

neutral and cold environments. The effect of adrenaline, though smaller than that of noradrenaline and isoprenaline, was not altered by hypoxia at either temperature.

3. It was concluded that the effect of the catecholamines on O_2 consumption in the cold and in hypoxia is complex.

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HEAT AS A LIMITING FACTOR IN ANIMAL PRODUCTION

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Abstract – The discussion is opened on the available methods of measuring heat tolerance. The importance of production level as being not only the final measurement of heat tolerance but probably the most sensitive as well is emphasized. Milk production under tropical conditions is described. Nutritional considerations when feeding under conditions of heat stress have been discussed in the light of recent developments in the field of ruminant nutrition. Original results in regard to the water metabolism of temperate and tropical cattle breeds have been presented and discussed. Reproductive failure in the tropics is discussed and the phenomenon of miniature births is presented in some detail. New evidence has been advanced from experiments carried out with a mutant woolly coated Afrikaner bull on the particularly important role of the hair coat in determining the heat tolerance of cattle. Finally original results in regard to environmental and endocrine factors which influence the character of the coat have been presented.

Zusammenfassung – Es werden verschiedene Methoden zur Bestimmung der Hitzetoleranz des Rindes beschrieben. Die Höhe der Nutzleistung ist nicht nur der Endzweck solcher Bemühungen, sondern wahrscheinlich auch der empfindlichste Anzeiger der Hitzetoleranz. Es werden Vorschläge gemacht für die Verbesserung der Milchproduktion in tropischen Gebieten durch die Anwendung geeigneter Haltungsmassnahmen. Fragen der Ernährung wärmebelasteter Tiere werden besprochen im Lichte der neusten Ergebnisse auf dem Gebiete der Wiederkäuerernährung. Es werden Resultate angegeben von Versuchen über den Wasserhaushalt von tropischen und europäischen Rindern. Im weiteren werden Fortpflanzungsstörungen in den Tropen besprochen, wobei die Geburt von „Miniaturtieren" speziell berücksichtigt wird. Gestützt auf Versuche mit einem durch Mutation entstandenen wollhaarigen Stier der Afrikanerrasse wird ein Beitrag gemacht zur Frage der Bedeutung des Haarkleides für die Hitzetoleranz des Rindes. Endlich werden einige Ergebnisse zitiert betreffend die Einwirkung verschiedener Faktoren der Umwelt und der inneren Sekretion auf die Beschaffenheit des Haarkleides.

Résumé – On décrit tout d'abord diverses methodes permettant de déterminer la tolérance des bovidés à la chaleur. L'importance du taux de production ne donne pas seulement la mesure finale de la tolérance à la chaleur mais qu'il en est probablement en outre le test le plus sensible. On propose des méthodes appropriées à l'amélioration de la production laitière en pays tropicaux. On discute également des questions de nutrition du bétail soumis à la chaleur et cela au vu des dernières constatations faites dans le domaine de l'affouragement des ruminants. On rapporte en outre le resultat d'essais effectués sur le métabolisme de l'eau de bovins d'origine européenne et tropicale. On relate des déficiences de la reproduction sous les tropiques, en tenant compte en particulier de la naissance de veaux nains. En s'appuyant sur des recherches faites au moyen d'un taureau au pelage laineux de la race africaine – taureau obtenu par mutation – on apporte une contribution au problème de la résistance au chaud par le pelage. Enfin, on cite quelques faits constatés de l'influence de quelques facteurs du milieu et des facteurs endocriniens sur le caractère du pelage.

INTRODUCTION

Although excessively high atmospheric temperatures have long been recognized as being a serious threat to successful livestock production, it is only comparatively recently that the biological implications have received serious scientific consideration. Moreover, in spite of the wealth of techniques which have been made available during the last decade for controlled research in psychrometric chambers, the general principles which were established some 20–30 years ago still hold good. These established principles have already been translated into practical policy with dramatic results and their application on the Continent of Africa will become increasingly important with the imminent population explosion.

Today with the advent of many elegant techniques and elaborate facilities the approach has become more basic and it is anticipated that through these studies our approach may be refined rather than revolutionized. The purpose of this paper then is to emphasize well established principles which can be applied with success, to indicate discrepancies requiring research and to report on unpublished results from this laboratory. The discussion will be conducted under the customary headings and will be restricted to the bovine.

HEAT TOLERANCE

The effect of thermal load upon respiration rate and rectal temperature was established many years ago and was used extensively by the earlier workers as a measure of heat tolerance. Rhoad (1944) used these findings to evolve the well known Iberian heat tolerance test which has been employed to assess the heat tolerance of various breeds, their crosses and the effect of age and other treatments upon heat tolerance.

Although there can be no doubt that temperate breeds will exhibit hyperpnoea and a rise in rectal temperature long before the tropical breeds when subjected to thermal stress it is felt that this criterion for evaluating heat tolerance is not sufficiently refined. It is our experience that under field conditions animals will show a significant drop in production long before marked stress symptoms such as hyperpnoea and hyperthermia are evident. Production, be it milk production or growth, is then not only the final measure but perhaps the most sensitive as well. Nevertheless production can only be measured accurately on a large scale and at considerable expense and techniques must be sought for a more refined evaluation of an animal's heat tolerance. Nitrogen and electrolyte balances as suggested by Kamal *et al.* (1962) seem promising but suffer somewhat from the elaborate techniques associated with balance trials. A rapid serological test would seem to be the goal and warrants further investigation.

GRAZING BEHAVIOUR

The fact that the normal grazing pattern under temperate conditions is almost reversed under tropical conditions was one of the first observations made at this Institute. The same observations have been reported by Seath and Miller (1946) and Payne *et al.* (1951). The important economic and managerial implications of this observation cannot be overemphasized for successful animal production in the tropics.

Among the less developed countries in the tropics it is standard practice to corral the animals at night either as a protection against predators or from lack of suitable fencing. It is at night, especially under semi-desert conditions where a sharp diurnal fluctuation in temperature is experienced, when most time is spent in grazing. Every effort should be made to provide these animals with night pasture as attested by the improved growth rate even among adapted breeds illustrated in Table 1.

Table 1. Comparison of the Live-Weight Records of Adapted Animals Corraled at Night and Those Allowed Free Range in Fenced Camps

	Camp system		Corral system	
Group	Average weight increase (lb)	Number of months	Average weight decrease (lb)	Number of months
I (30)	+35	2	−84	2
II (37)	+15	3	−65	1

NUTRITIONAL CONSIDERATIONS

Apart from earlier work by Robinson and Lee (1947) the direct effects of nutrition upon heat tolerance in ruminants remains a relatively neglected field. Associated fields of study have, however, expanded swiftly in recent years especially in regard to the energy metabolism of the ruminant (Blaxter, 1962). An integration of ideas in this respect would be of undoubted advantage.

It has for example been shown that by manipulating the concentrate to roughage ratio the ratio of the volatile fatty acids in the rumen are altered. The question now arises – will this alteration in volatile fatty acid production influence the heat load significantly via the heat increment to make it a practical consideration in feeding for heat tolerance? Under practical conditions economic considerations dictate feeding policy and roughage with its associated high heat increment must by necessity be fed or grazed in large amounts. The advent of pelleted roughages, however, alters the picture somewhat and it is felt that this would be a rewarding field of investigation for the environmental physiologist.

Bonsma (1961) has reported the success which has been attained in Israel dairy herds with heavy concentrate feeding and a minimum of roughage under conditions of high ambient temperatures. It remains to be elucidated to what extent this is due to altering the energy balance via the heat increment and volatile fatty acid production in the rumen.

MILK PRODUCTION

There is no doubt that milk production represents the most efficient conversion of nutrients for human nutrition. The high metabolic requirements for efficient milk production are, however, antagonistic to the provision of a low heat load to provide heat tolerance in cattle. Various efforts have been made to breed heat tolerant dairy cattle by crossing the well known dairy breeds with indigenous African and Asian cattle. These efforts have at best resulted in a reasonable compromise because of the contradictory metabolic implications. It is felt therefore that milk production should be avoided whenever possible under conditions of high thermal stress. When economic considerations demand that milk be produced under these conditions the solution may best be sought in improved management practices rather than through breeding.

It is the experience of this Institute that reasonably efficient milk production can be maintained under conditions of high ambient temperature with the recognized dairy breeds provided management is of a high order. The following managerial practices have been found to be particularly effective: the provision of complete shade during the day in conjunction with water sprinklers, the heavy feeding of concentrates as opposed to coarse roughages, the feeding of pelleted roughages, the limiting of muscular activity especially walking, protection against biting and stinging insects and the provision of succulent night pasture with a low cellulose content. An exact quantitative assessment under controlled conditions of the relative value of these practices remains to be done. This is especially true of the nutritional regime as outlined in the discussion on nutritional considerations.

WATER METABOLISM

The effect of thermal stress upon water consumption of various breeds has been throughly investigated in the last two decades and notably by the Missouri group under Brody. These effects have been reviewed by Findlay (1954). A quantitative assessment of total water balances and the associated electrolyte balances has, however, received surprisingly little attention until recently (Kamal *et al.*, 1962, MacFarlane *et al.*, 1958).

In view of the arid or semi-arid conditions which frequently prevail in territories experiencing high atmospheric temperatures a basic understanding of total water balance, together with an appreciation of breed differences in this respect, is of the utmost importance. It has also always been assumed from practical field observations that the indigenous Afrikaner breed is a far more efficient utilizer of water than the temperate breeds — the exact nature of this superior efficiency is, however, not clear.

Recent work at this laboratory has attempted to contribute to this problem by comparing the partial water balance of Afrikaner and Shorthorn steers at high ambient temperatures (90° F). Under conditions of semi-controlled water intake which approximate practical conditions more closely than *ad libitum* it was found that surprisingly little difference in the total water balance between these breeds, as measured by water intake and excretion of water in the urine and faeces, occurred. Although little difference was observed in total balance a significant difference in the pathways whereby moisture loss occurred was apparent (Table 2).

Table 2. Comparison Between the Partial Water Balance of Afrikaner and Shorthorn Cattle at 90° F over an Experimental Period of Five Days

Breed	Water intake l.	Water loss in urine l.	Water loss in faeces l.	Total loss in urine and faeces l.	litre water loss in urine and faeces per litre intake
Afrikaner	875	145	235	380	0.434
Shorthorn	991	171	279	450	0.454

Although both breeds exhibited an increased urine volume at high ambient temperatures no breed differences were apparent in this respect. A statistically significant difference in faecal moisture was, however, recorded. The Afrikaner breed lost significantly less moisture via this pathway than the Shorthorn. Moreover, on withholding both water and feed from the animals it was observed that the faecal moisture dropped far more rapidly in the case of the Afrikaner. It would appear then that the Afrikaner, similar to many desert animals, is capable of a measure of moisture conservation via this pathway. Under the temperature conditions of the experiment (90° F) the Afrikaners were able to maintain normal rectal temperatures and did not exhibit hyperpnoea. They were observed, however, to sweat freely under the metabolism harness. The Shorthorns on the other hand showed minimal sweating activity and exhibited thermal stress as judged by rectal temperature and respiration rate. The moisture loss via sweating on the part of the Afrikaner was in all likelihood balanced by the respiratory loss of the Shorthorn exhibiting hyperpnoea to give a similar total overall balance for both breeds (Table 2). These differences in the pathways whereby moisture is lost is then associated with the superior heat tolerance of the Afrikaner breed. A more refined approach designed to include measurements of total body water, blood volumes and the various water spaces is indicated.

REPRODUCTION

The deleterious effects of tropical and sub-tropical environments upon the reproduction of temperate breeds under field conditions was recognized and described at the turn of this century. Adequate reviews of the problem are contained in Cole and Cupps (1959) and Ulberg (1958).

It is now well established that bulls of the temperate breeds exhibit a rapid decline in fertility when exposed for prolonged periods to high ambient temperatures. Apart from the cessation of spermatogenesis as a result of body temperatures of 106° F and scrotal temperatures of 115° F the scrotum becomes pendulous and very prone to permanent injury. The Afrikaner, on the other hand, possesses a scrotum with a skin thickness twice that of the temperate breeds and with increasing ambient temperature the scrotum becomes retracted, the skin becomes puckered and is consequently a poor conductor of heat. Moreover, the testes are retracted against the perivisceral cavity so that their temperature does not rise above that of body temperature which is seldom higher than 102.5° F in the case of the Afrikaner (Bonsma, 1940).

The great economic importance of fertility levels in determining the turn-over in any animal production enterprise requires that this aspect of reproduction, viz. the effect of heat on spermatogenesis should receive far more detailed attention than has been the case. For example what are the effects of short term temperature fluctuations which exceed the critical temperature for only a matter of hours in so-called temperate regions? In fact, what are the exact critical temperatures and critical periods of exposure which are required to interfere with normal spermatogenesis?

Unadapted female cattle exhibit very low fertility and frequently complete sterility under conditions of thermal stress. Under extensive ranching conditions these animals also exhibit a marked voluntary anorexia in order to minimise their heat load and to reduce the muscular activity involved in foraging. The question now arises to what extent is the reduced fertility due to malnutrition and the resultant degeneration, and to what extent to direct effects of hyperthermia upon the reproductive process. Undoubtedly both factors are involved but it is surprising how limited our knowledge is in regard to climatic influences upon specific forms of female reproductive failure. Van Rensburg and De Vos (1962) working on cattle in this country have demonstrated seasonal effects upon ovulatory failure but only within a temperate zone. In spite of earlier work on sheep by Yeates (1953) and Alliston and Ulberg (1957) a more exact assessment of the effect of thermal stress upon ovulatory failure, fertilization failure and embryonic loss in the bovine is urgently required. Again, critical temperatures should be sought for later practical application.

FIG. 1. Miniature Shorthorn Calf compared with normal Afrikaner Calf

A most interesting form of reproductive abnormality due to heat stress recorded at this Institute is the birth of miniature calves. These calves are born to unadapted cows of the temperate breeds whose gestation period coincides with the hottest months of the year. The weights of these calves range from as low as 19 lb to 52 lb (Fig. 1). Interesting also is the fact that bull calves of this type are significantly lighter than the females. Although the dams of these calves are by necessity on a low plane of nutrition as a result of a measure of voluntary anorexia the nutritional plane cannot be considered as the primary cause of this phenomenon as it has been shown that the nutritional plane can vary within very wide limits before birth weight is affected (Joubert, 1954). A rational explanation of the physiological implications of this phenomenon may contribute valuably to the problem of reproductive failure under heat stress as a whole.

NATURE OF THE HAIR COAT

Bonsma (1943) and Riemerschmid and Elder (1945) drew attention to the importance of coat colour for reflecting solar radiation and thereby providing protection against the intense solar load experienced under field conditions. In spite of these convincing results coat colour has as yet not become an important practical consideration in breeding cattle for heat tolerance. Anyone who has had experience of handling cattle of different coat colours under high temperature conditions needs no convincing of the importance of this characteristic and it is difficult to understand why these principles have not enjoyed general acceptance in practical breeding policy. A possible reason is that the available indigenous breeds as well as their crosses have given sufficiently good results without attention to this factor. Furthermore, comparative research on this factor is handicapped by the fact that colour comparisons always involve breed comparisons. This is, however, being overcome at this Institute by crossbreeding Angus cattle with the indigenous N'guni breed and Afrikaner. The reciprocal crosses of the offspring of these breeds provide a range of colours from coal black through silver grey to light cream with similar genetic composition thus providing excellent material for these investigations. Colour, though not as important as texture of the coat, remains an important consideration in breeding for heat tolerance and warrants far more attention than it has received in the past.

The senior author established the importance of the texture of the hair coat in providing heat tolerance to cattle some 20 year ago (Bonsma and Pretorius, 1943). After 20 years of experience in selecting, breeding and handling cattle in the tropics and sub-tropics it is his considered opinion that this factor is the most important single morphological characteristic that determines the heat tolerance of cattle breeds – far more so than for example conformation, area of skin surface per unit weight and distribution of body fat. At the Mara Research Station it has been possible through strict selection for sleek and glossy coats to develope a herd of smooth-coated Herefords whose performance compares favourably with that of the indigenous breeds and their crosses.

As with coat colour comparative research on this aspect is handicapped by the involvement of breed differences. Some years ago this Institute was, however, fortunate in obtaining a woolly coated Afrikaner bull. Normally when Afrikaners are crossed with British breeds the sleek smooth coated characteristic of the Afrikaner is dominant and appears in the F_1 – these progeny are then heat tolerant. The mutant woolly coated Afrikaner bull on the other hand threw both woolly coated and smooth coated calves when crossed with British breeds. The growth rate of the steers obtained from these crosses (all of them either sibs or half sibs) has been studied under tropical conditions at Messina Research Station.

These results (Table 3) illustrate very convincingly the great importance of the nature of the hair coat and the experiment has the distinct advantage of appraising the growth rate of animals with a similar genetic background and not different breeds. From the results in Table 3 and Figs. 2 and 3 it can be seen that even after 7–8 years there is a tremendous difference in liveweight. In view of the great importance of the character of the coat this Institute has carried out a series of experiments in order to obtain a clearer understanding of the factors influencing this characteristic.

Table 3. Comparison of Growth Rate Between Smooth Coated and Woolly Coated Half Sibs Sired by the Same Mutant Woolly Coated Afrikaner Bull

Coat type	Average birth weight (lb)	Average weight at 2yr (lb)	Average weight at 4yr (lb)	Average weight at 6yr (lb)
Smooth coated	74	675	875	1165
Woolly coated	53	325	475	690

An important fact which has emerged from these studies is that the nature of the photoperiodic gradient is an important factor influencing the hair shedding mechanism. Yeates (1954) has advanced the opinion that a slow continual change in the

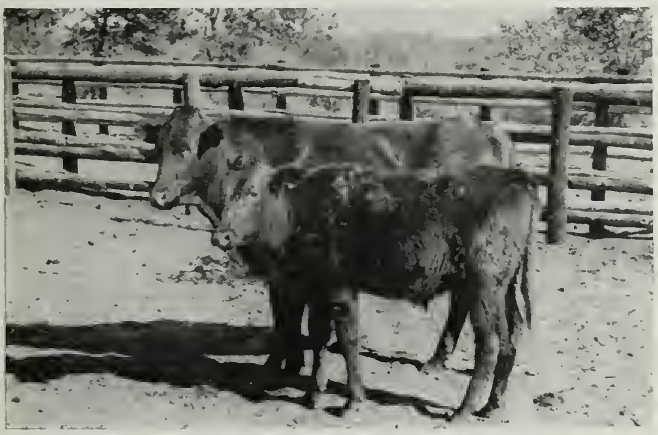

FIG. 2. Afrikaner Shorthorn
A1 – Smooth Coated
Age, 1 year
Weight, 505 lb

Afrikaner Shorthorn
A3 – Woolly Coated
Age, 1 year
Weight, 300 lb

gradient is more effective than large sudden changes. Our studies which were designed to investigate the effectiveness of a large sudden change in the photoperiod followed by a gradual change in the opposite direction showed that the sudden change was more effective in evoking the hair shedding mechanism. This fact can be applied in practice to bring bulls of the temperate breeds, that are being used for crossbreeding in the tropics, into a sleek summer condition for the early spring breeding season. The ideal treatment would appear to be a sudden large increase in daylight length during autumn which is followed by a gradual increase (10 min/week) throughout the winter.

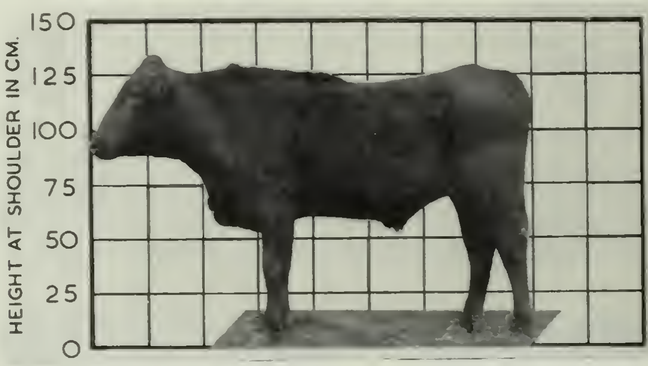

Fig. 3. *No. A1.* Date of birth 2/1/56. Photographed 2/5/63 – Age $7\frac{1}{2}$ yrs. Height at shoulder 151 cm. Weight 1800 lbs

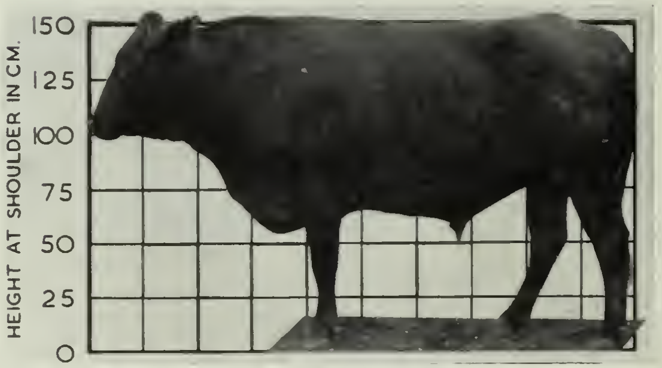

Fig. 3. *No. A3.* Date of birth 7/2/56. Photographed 2/5/63 – Age 7.4 yrs. Height at shoulder; 124 cm. Weight 830 lbs

A further fact of importance to emerge from these studies is that, although the photoperiod is of great importance in influencing the hair growth and shedding mechanisms, ambient temperature appears to fulfil an important function as well. This is especially true when the animal is in a good state of nutrition but the relative importance of the two factors cannot be unravelled at this stage.

During these studies tentative evidence was obtained to show that a high thyroid stimulating hormone (TSH) content of the anterior pituitary was positively correlated with the length of the hair coat. Conversely, length of hair coat was found to be negatively correlated with the pituitary gonadotrophin content. The latter observation is in agreement with earlier work on a small scale at this Institute which showed that heifers responded to PMS injections by shedding their winter coat. The physiology of the hair growth and shedding mechanism is receiving considerable attention today – it certainly deserves this attention. In closing the authors would like to emphasize that, although heat is the most dramatic factor affecting animal production in the tropics, other environmental factors are of great importance. The approach of the animal scientist concerned with this problem must therefore be via the total environment. Moreover, although the expanding field of environmental physiology studies in psychrometric chambers has and will contribute greatly to our basic understanding of the problem, field studies on an extensive scale must provide the final answer. In psychrometric rooms the solar load is absent, the walking and foraging ability of the animal is not considered nor its resistance to disease and ecto- and endoparasites. In spite of this it is disappointing to note that extensive field studies have not kept pace with the rapidly expanding research in psychrometric rooms.

It is difficult to overemphasize the importance of environmental studies in the field of animal production. Vast areas of Africa and Asia are threatened with overpopulation and due to the arid and semi-arid conditions prevailing in these territories agriculture is often limited to a primitive pastoral economy. Present day knowledge, especially in regard to judicial crossbreeding and management, is sufficiently far advanced to bring about dramatic improvements in these countries. The problem is therefore largely one of education.

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THE THERMOREGULATORY SIGNIFICANCE OF THE HAIR COAT, WITH SPECIAL REFERENCE TO CATTLE

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A COMPARISON was made in the semi-arid region of Queensland of three groups of cattle, possessing different types of hair coats: (A) short, sleek ("adapted") coats, (B) partially shed coats, and (C) coats that had not been shed ("Wintercoats").

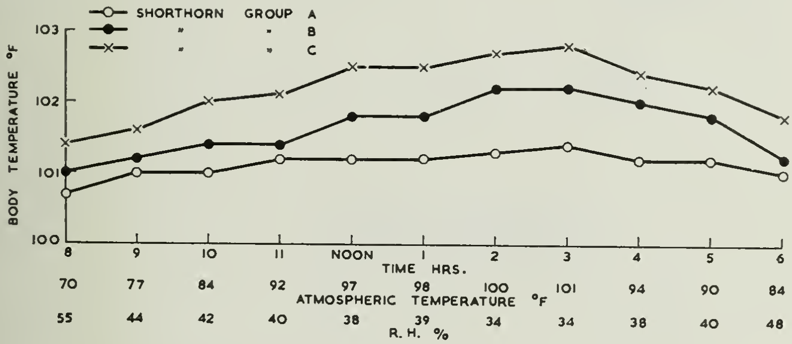

FIG. 1.

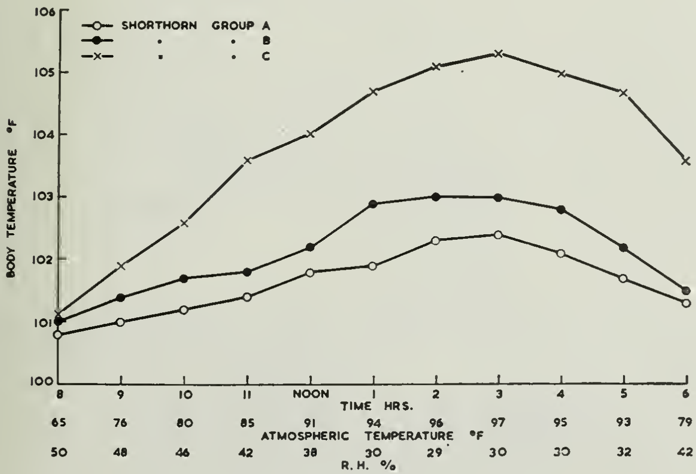

FIG. 2.

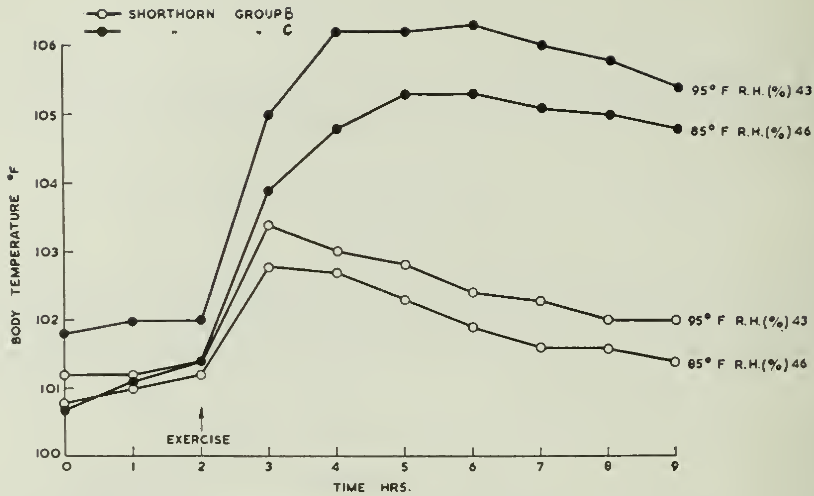

FIG. 3

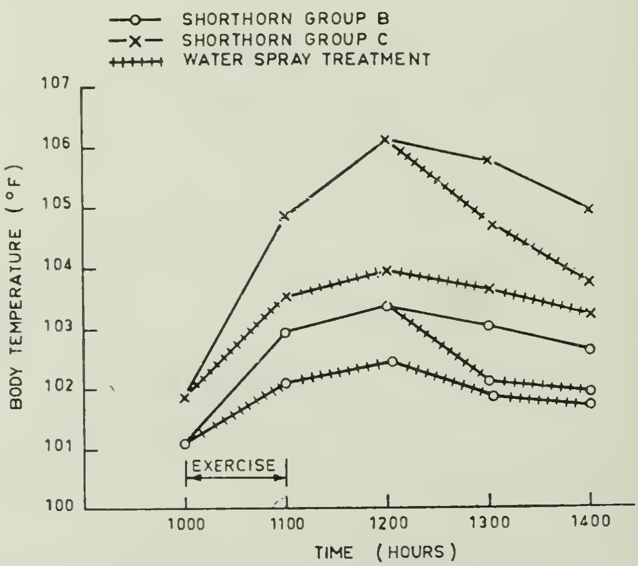

FIG. 4. Body temperature Regulation in Cattle.
Effect of wetting coat with water spray.
(Rainsby Shorthorns exp. 21)

Under various conditions of heat stress, group (A) animals showed the highest, group (C) animals the lowest heat tolerance as judged by the behaviour of rectal temperature. This is evident from the following figures:

Figure 1. In a hot environment, but sheltered from direct solar radiation, a small difference in heat tolerance was apparent between the groups.

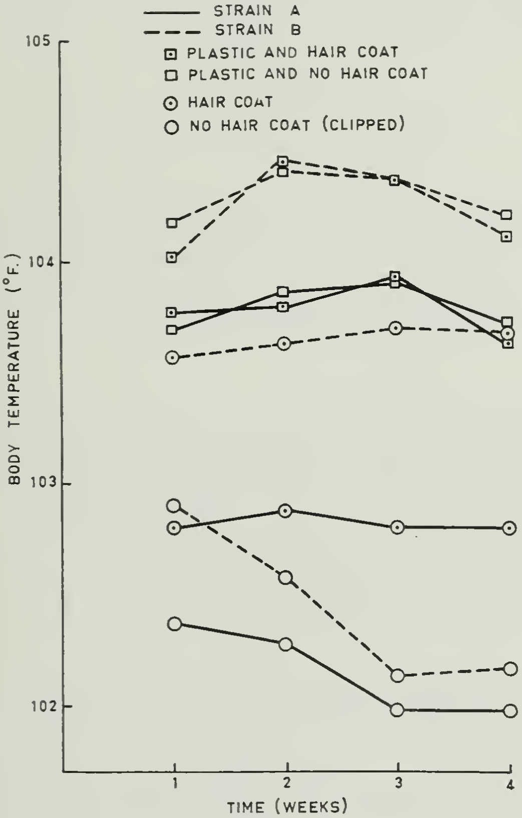

Fig. 5.

Figure 2. Exposure to heat plus solar radiation enhanced these differences, particularly with respect to group (C).

Figure 3. Exposure to the accumulative stress of heat, solar radiation and physical exercise led to a clear differentiation between the groups (B) and (C). Group (A) animals were not included in this test since they might not have survived it.

Figure 4. Wetting the coats of the animals with a water spray significantly lowered body temperature, but group differences remained.

Figure 5. Clipping the coat decreased heat strain; covering the animals in plastic coats increased it. Plastic coats made of reflective material were slightly less deleterious in their effect than those made of transparent material.

The observed differences in heat tolerance between the groups were thought to be due mainly to the degree of interference of the hair coat with evaporation from the skin.

A CONTRIBUTION ON METHODS OF INVESTIGATING THE EFFECTS OF WEATHER AND CLIMATE ON FARM LIVESTOCK UNDER NORMAL MANAGEMENT IN THE BRITISH ISLES

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Abstract – It was emphasized that in field studies designed to evaluate the effects of meteorological factors on farm animals the physical measurements should be properly matched to the biological measurements. Recent work on the energy balance of cattle and sheep indicated that the response times of various physiological parameters were such as to permit the use of conventional meteorological apparatus. Sampling meteorological variables over periods of 1 hour could provide biologically meaningful information. Data were presented from a field survey in North Wales on the effect of the ground contour on the surface wind.

Zusammenfassung – Es wurde auf die Notwendigkeit hingewiesen, beim Studium der meteorologischen Einflüsse auf landwirtschaftliche Nutztiere die physikalischen und die biologischen Messungen miteinander in Einklang zu bringen. Neuere Untersuchungen auf dem Gebiete des Energiehaushaltes beim Rind und Schaf deuten darauf hin, dass die Reaktionszeiten verschiedener physiologischer Grössen von einer Grössenordnung sind, welche die Verwendung konventioneller meteorologischer Apparate gestattet. Die Integrierung meteorologischer Grössen über 1-stündige Perioden ist geeignet, biologisch zweckvolle Angaben zu vermitteln. Es wurden Ergebnisse eines Feldversuches in Nord Wales mitgeteilt über den Einfluss der Geländekonturen auf den Bodenwind.

Résumé – On insiste sur la nécessité d'accorder les mesures physiques et biologiques lors de l'étude des effets météorologiques sur les animaux domestiques. Des études récentes dans le domaine du bilan énergétique des bovidés et des moutons montrent que les temps de réaction de différentes valeurs physiologiques sont d'un ordre de grandeur tel qu'ils permettent l'usage d'instruments métérologiques conventionnels. L'intégration durant 1 heure de grandeurs météorologiques permet d'obtenir des indications biologiquement valables. On communique ici les réultats d'un essais destiné à montrer l'influence des contours du terrain sur le vent, essais fait en plein air en Galles du Nord.

GENERAL CONSIDERATIONS

We are dealing with the interaction between a physical and a biological system, and basically the problem of experimental design resolves itself into one of *sampling* in time and space – using the term in its broadest sense.

To investigate the response of a biological system to physical stimulae, it is necessary that what is known of the scale, rhythms, tolerances etc. of the biological system should be clearly stated, in order to derive an appropriate experimental design for the physical measurements. In view of the subject matter of our Second Plenary Session only brief mention of time-variations is called for in this paper.

Initially, we may regard "field-scale" biological events as:

extensive in time and space;
or extensive in one aspect, but limited in the other;
or limited in both aspects.

Meteorological events linked with a doubly-extensive occurrence (such as disease outbreaks affecting plants or animals over tens or hundreds of square kilometers and lasting for several weeks or months), must in general be identifiable from *mean* values of once daily or less frequent observations from a representative, but *open*, network of weather observing stations. By contrast, phenomena occurring within an area of a few hectares and within a period of 24 or 48 hr e. g. local frost damage, require a closer network and more frequent (at least once daily) observations for their investigation.

In recent years the general recognition of the very large spatial gradients of temperature, humidity and air flow which can occur within the first few tens of centimeters from a surface, has thrown doubts on the possibility of a successful attack on a wide range of biometeorological questions by the use of the gross weather parameters from a conventional climatological observing network. Such doubts can be exaggerated: often, either the relevant "macro"-situation is associated with small "micro"-meteorological variations (as with conditions favourable to Potato Blight — see Bourke, 1962), or it permits an adequate range of favourable "micro"-conditions to occur with sufficient frequency as illustrated, for example in a study by Williams (1961) of insect populations and activity.

At the outset, it is desirable to stress that our aim is to develop techniques for exploiting fundamental results for the benefit of commercial agriculture. For this to be achieved it must be made possible to assess the properties of the physical environment of any area by:

(i) "on-site" and map studies of the land form and surface "roughness";
(ii) short-period meteorological and other surveys using simple instrumentation and simple field techniques, not involving the attendance of even non-skilled persons more frequently than (say) twice a week;
(iii) employing such synoptic and climatological aids as are available: the whole carried out to that degree of precision which is biologically meaningful in the context of commercial operation.

PROVISIONAL SPECIFICATIONS FOR FIELD INSTRUMENTS

Calorimetric studies with sheep and cattle (Blaxter, Graham, Wainman and Armstrong, 1959; Gonzalez-Jimenez and Blaxter, 1962; Blaxter and Wainman, 1961) and studies of the energy exchange of sheep in the field (Joyce, 1963; Joyce and Blaxter, 1964) have established the following general principles.

(a) The surface temperature of the extremities of animals (ears, feet and legs) respond very rapidly, that is in a matter of minutes, to ambient conditions. These reactions involve restriction of the blood supply to the skin and extremities. In response to cold, once these changes in blood supply are complete, animals increase their metabolism to maintain constant body temperature. This adjustment is termed a metabolic adjustment and occurs only when the animal's blood vessels are constricted.

(b) With sheep having fleeces up to 3–4 cm in effective depth, virtually complete metabolic adjustment is attained following sudden changes in climatic variables as set out below:

(i) For changes in ambient temperature – about 30 min;
(ii) For changes in air speed – about 40 min;
(iii) For changes in the intensity of infrared radiation – about 50 min;
(iv) For changes in the intensity of solar radiation – about 15 min (but this interval may change with fleece length).

(c) Significant changes in heat production of vaso-constricted animals can be elicited by changes of 0.5° C in air temperature, by changes of 0.5 m/s in air speed in the range 0–5 m/s, and by 0.05 Langleys for solar radiation at low total intensities. With rain, penetration of the hair coat (cattle) leads to large increases in heat loss, but once the coat is wet, losses appear then to be little affected by the amount of subsequent rain.

These observations suggest the following as realistic proposals for the recording of the meteorological data for even the most detailed of field studies likely to be undertaken with sheep and cattle under commercial conditions.

(i) Variables should be integrated over hourly periods:
(ii) In principle, the instrumental systems available to ordinary climatological stations in the U.K. are capable of measuring air temperature, humidity, precipitation and wind speed with the required accuracy (we lack a suitable wind direction recorder). Two instruments would be needed to cover the full range of wind-speeds, unless the tolerances can be widened to ± 1 m/s as indeed field variability might dictate. All recording systems must work unattended for at least one week.
(iii) There appear to be no suitable systems for recording short- and long-wave radiation. Twenty-four hour *totals* of short-wave input can be obtained, and comparative, if not absolute, values of radiation components computed

from statistical relationships, whilst observations from "probe" instruments such as the globe-thermometer (see Brooks, 1959) can provide some relevant data.

SOME ASPECTS OF A STUDY OF AIR-FLOW IN HILLY AREAS

As a contribution towards developing techniques for field investigations in hilly areas, some features of a current investigation at the College Farm, Bangor (see Figs. 1 and 2) will be considered. No new principles are involved, but some progress towards precision may emerge.

Although much is known on the subject of wind and shelter ("The Effects of Windbreaks and Shelterbelts" World Met. Org. Bulletin 1962); there are gaps in our knowledge of how certain features of the landscape (which present various degrees of "aerodynamic roughness"), affect the flow. Conveniently we may think of "macro" roughness, when considering areas of hundreds of thousands of km^2 in extent; the "meso" roughness of the isolated hill or forest, etc.; and the "micro" roughness presented by tree belts, hedges, boulders, vegetation etc. where a linear scale of meters, or even centimeters, is appropriate.

An important and critical feature of "meso"-scale surface air-flow is whether or not there is break-away from the surface. Gloyne (1959) has presented evidence which suggests that except when inversions are present, the air-stream will not follow a rising slope of more than about 30° to the horizontal nor a descending slope of more than 10° (other work indicates a value less than 10°, W.M.O. Tech. Note 1963).

Within the limits imposed by practical considerations, the layout of the anemometers on the hill, viz. Nos. F. 1, 2, 3, 4, 5 (see Fig. 2) was governed by the needs:

(i) To permit specification of the surface wind before, during and after the shelter-belts constitute significant features of the terrain;

(ii) To ensure a control site (Station F) which would be unaffected by the growing belts — at least for a range of incident wind conditions;

(iii) To provide some measure of replication under any specified incident wind direction;

(iv) To take account of the presumed importance of the angle of slope on surface flow.

In addition, the schedule of observations and the methods of analysing the information were such as to take full advantage of observations of daily run-of-wind at the College climatological station L (see Fig. 2), and of data from the anemograph at Valley Airport Station V (see Fig. 1). Except for Station V the wind was measured at 2 m — a level closely related to the zone occupied by livestock; and one where the air-flow would be significantly affected by the shelterbelts, but largely uninfluenced by fortuitous features of the surface of the ground within several metres of the instrument.

The data examined below are based on total wind-run over periods of 2 to 4 or 6 days during which time the mean gradient wind direction did not differ by more than about ± 5° from the decadal values 010°, 020° . . . (see Table 1). During these

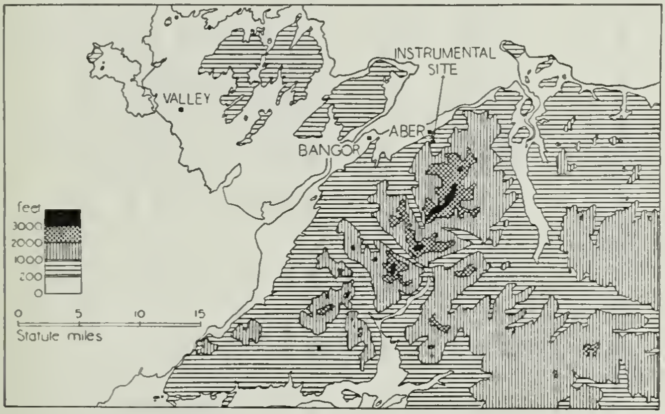

Fig. 1. Topographical map of part of North Wales and Anglesey

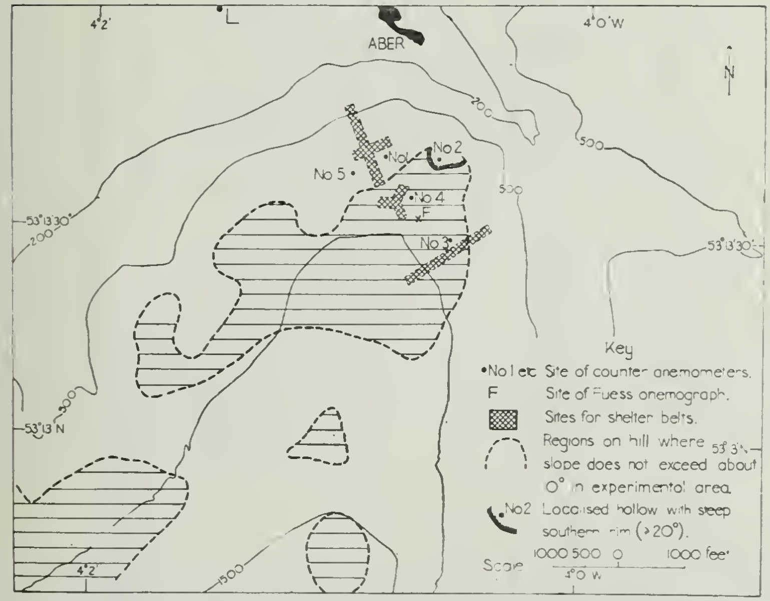

Fig. 2. Layout of anemometer network at College Farm, Bangor, N. Wales

Table 1. Comparisons of Wind Velocity on the Experimental Farm (University College, N. Wales) March 1960 – March 1961

	Direction – in degrees from North																		
Gradient Wind	050	070	090	120	130	140	150	160	170	180	190	200	210	220	230	240	250	260	270
Station V	010	050	060	090	85	95	115	125	145	175	175	190	200	205	215	230	240	260	260
Station F	015	070	110	115	125	120	130	160	155	130	175	200	200	200	200	215	220	210	230
Ratio	*Wind-run at Station F (h = 2m)/gradient wind-run*																		
R (2m at F)	0.50	0.55	0.55	0.55	0.65	0.55	0.70	0.30	0.45	0.50	0.35	0.35	0.45	0.40	0.40	0.45	0.30	0.40	0.40
Station	*Wind-run as Percentage of that at Station F*																		
F	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
V(a)	65	75	40	40	50	55	20	50	60	50	80	105	110	110	115	85(b)	140(b)	100	100
L	75	75	60	45	50	55	50	70	60	60	70	70	85	90	90	90	115	90	120
1	100	100	90	70	70	70	75	80	75	80	80	90	85	95	100	100	120	110	–
2	70	80	75	70	65	65	75	60	75	75	65	70	65	70	70	75	85	65	80
3	105	100	100	100	95	95	95	100	100	105	105	110	105	110	110	110	120	100	110
4	100	100	100	95	90	95	95	95	90	–	80	90	85	90	90	95	110	160	110
5	100	95	90	70	70	75	85	95	80	95	115	105	105	110	115	115	135	125	130

(a) Reduced to speed at 2m.
(b) Airfield obstructions might be responsible for anomalous values

spells, wind directions at station F were confined to a small directional range, but less markedly so at V; and the average daily wind-run at F ranged from a little below 300 km to a modal value of about 550 km. The method of selection tended to eliminate situations with light winds, i.e. those in which large thermal gradients are most likely to occur.

Some features revealed by the information in Table 1, Figs. 1 and 2 are:

(i) Wind direction at V compared with that of the gradient wind agrees with expectation, except for gradient directions spanning 190° to 220° when deflection of flow by the hill mass is indicated.

(ii) At F we note coincidence of surface and gradient direction at 200° but an increasing backing at F to 200°–220° as the free wind veers from 200° to 270°, and the association of winds between 110° and 130° at F with a gradient from 090° to 150°.

(iii) Exceptionally for easterly gradients wind-run at station 2 was less than at any other hill station. The exceptions arise when the incident wind is not forced to descend the steep ($> 20°$) rim of the hollow.

(iv) With different incident wind direction, different groups of instruments become replicates e.g. Nos. 1, 4, 5, F with a gradient of 070°.

(v) A deflection of wind along the flanks of the hill is illustrated by the association of surface directions of 110°–130° and 200°–220° with gradient directions respectively of 070°–150° and 200°–260°.

(vi) With easterlies, Nos. 1 and 5 return values lower than No. 3, whereas with gradient 220°–270° (200°–210° at F), No. 3 records values similar to No. 5 and exceeding No. 1. The differences are consistent with arguments based on slope angles, but, lacking wind direction observations at No. 3, "funnelling" along the valley to the east of the station cannot be ruled out.

This study indicates that many of the main characteristics of the air-flow in hilly areas can be revealed by surveys involving simple counter anemometers and one "control" instrument which can provide the principal features of a continuous record of wind velocity.

If the sampling interval is not less than about 48 hr, a 12-month survey may be necessary, but the period can be much reduced given a sufficiency of 24-hour runs. It is the writer's conviction that, based on knowledge gained from the results of a number of similar surveys, it should be possible to infer the basic features of surface wind regime at any site from: one-site inspection; instrumental surveys for periods reckoned in days or weeks rather than months; and the associated synoptic and climatological analysis.

PROPOSALS

1. Any Code of Practice for biometeorological investigations should require explicit consideration of rhythms, spatial and temporal variations and tolerances, of both the physical and biological systems.

To the extent that classes of situations arise, meteorologists should be prepared to assemble basic data in appropriate forms.

2. Some priority should be given to the development of robust instrumental systems based upon modifications of conventional, and therefore readily available equipment, A parallel effort is needed with respect to procedures and techniques of analysis and presentation.

3. Recognizing the importance of the form of the land surface, terrain should be classified according to its geometry, initially with emphasis on slope. The basis of classification will depend on how the terrain influences the physical (or biological) element under consideration.

4. Field surveys, together with supporting climatological and synoptic analysis, should be undertaken in selected sites of definable geometry, using a variety of instrumental systems, procedures and sampling networks.

5. Measures for the collection, publication and circularizing of useful information should be strengthened.

ACKNOWLEDGEMENTS

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THE ZONE OF THERMONEUTRALITY IN SWINE ON FULL FEED*

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Abstract – Total heat loss from 43 groups of hogs has been measured by converting the California Psychrometric Chamber to an air calorimeter. These hogs were on full feed during the experiments. Experimental periods were for 7 days, and calorimeter measurements were made of the heat removed from the Chamber during the last 2 to 3 days of each period. Minimum heat loss values were obtained from 26.7° C for 22.7 kg hogs to 33.3° C for 90.7 kg fed hogs. For heavier hogs up to 180 kg, the heat loss curves did not show minima in the ambient temperature range of 4.4° to 37.8° C. There were no clear-cut breaks in heat loss curves to delineate zones of thermoneutrality. The ambient air temperatures at which most rapid gains have been reported are somewhat lower than the temperatures for minimum heat production of fed hogs, and the change with different body weights is in an opposite direction.

Zusammenfassung – In einem Luftkalorimeter (entstanden durch Modifikation einer Klimakammer) wurde im Temperaturbereich 4.4–37.8° C die Gesamtwärmeabgabe von 43 Gruppen von normal gefütterten Schweinen gemessen. Die Messungen erstreckten sich über die letzten 2–3 Tage 7-tägiger Versuchsperioden. Tiere der Gewichtsklassen 23 kg und 91 kg hatten Minima der Wärmeabgabe bei Lufttemperaturen von 26.7° und 33.3° C. Tiere höherer Gewichtsklassen (bis 180 kg) zeigten keine Minima. Die Kurven für die Wärmeabgabe liessen keine deutlichen Zonen thermischer Neutralität erkennen. Die hier festgestellten Temperaturen für minimale Wärmebildung gefütterter Schweine liegen etwas höher als die Temperaturen für maximale Gewichtszunahme; ausserdem verändern sich in den beiden Versuchsreihen Gewichtsklassen in umgekehrter Richtung.

Résumé – On a mesuré au moyen d'un calorimètre (chambre climatique modifiée), la perte totale de chaleur de 43 groupes de porcs normalement nourris et cela entre 4,4° et 37,8° C. Les mesures furent effectuées durant les 2 à 3 derniers jours de périodes d'essais de 7 jours chacune. Les bêtes des classes de 23 et 91 kg avaient un minimum d'émission thermique pour des températures de 26,7° et 33,3° C. Les bêtes dépassant ce poids (jusqu'à 180 kg) ne présentaient pas de minimum. Les courbes de perte de chaleur ne permettent pas de fixer des zones nettes thermiquement neutres. Les températures déterminées ici pour la moindre production de chaleur sont légèrement supérieures à celles permettant les plus forts gains de poids. En outre, les classes de poids se comportent en sens opposé dans les deux séries d'essais.

MEASUREMENTS of the zone of thermoneutrality, sometimes called the comfort zone, are many times reported on the basis of heat production or metabolism measured

* This report is one of a series resulting from a cooperative project between the United States Department of Agriculture and the University of California at Davis.

under basal or resting conditions (Brody, 1945; Kleiber, 1961). In this zone environmental temperature is theoretically perfectly adjusted, and body temperature is maintained at a normal level with little or no chemical regulation. Physical regulation of body temperature occurs. Below the lower critical temperature chemical regulation becomes necessary to maintain body temperature. This point may be considered as the lower limit of the zone of thermoneutrality (Brody, 1945).

Tangl (1912) estimated that the lower critical temperature for pigs weighing 50 kg was between 20° and 23° C. For pigs weighing 100 kg he estimated that it was less than 16° to 17° C. Under their conditions, Capstick and Wood (1922) estimated that the lower critical temperature was 21° C for a hog weighing 136.1 kg. Deighton (1929) studied the heat production of a hog which weighed from 7 to 200 kg and concluded that its critical temperature was 16° C. While these studies are not in complete agreement, they do give an idea of the lower critical temperature of the pig. They show that it is affected by body mass, and indicate the lower limit of the zone of thermoneutrality for a fasting hog.

Brody (1945, p. 295) has commented that "Interesting as these 'critical' values may be theoretically and for research purposes, they are probably without significance for normal farm animals under normal management conditions." Thus Kleiber (1961, p. 274) has indicated different critical temperatures for fasting and fed animals. The difference is due to the calorigenic effect of food.

If the critical temperature is affected by feeding, so is the zone of thermoneutrality. From the swine grower's standpoint, the zone of the fed pig is the one of most importance. Presumably, such a zone would be the area where swine would perform most efficiently with ambient temperature as a variable. Working in the California Psychrometric Chamber (Heitman, Kelly, and Hughes, 1949), with constant ambient temperatures, the optimum ambient temperatures for maximum gain in weight of swine varied from 16.1° to 23.1° C for hogs weighing from 158.8 to 45.4 kg, respectively (Heitman, Kelly and Bond, 1958). It might be expected that such temperatures should be about the same as for optimum feed conversion (Heitman and Hughes, 1949). In general, such temperatures approximate or are slightly higher than those reported for the lower critical temperatures for swine of similar weight. One of the noteworthy observations in the California studies was the rapidity with which gain fell off with relatively small ambient temperature changes on either side of the optimum. The zone of thermoneutrality, as ordinarily shown in graphs (Brody, 1945; Kleiber, 1961), is a much flatter kind of a curve than that pictured in the curve showing weight gain against ambient temperature (Heitman *et al.*, 1958).

MATERIALS AND METHODS

The data considered in this report were reported as part of another study by Bond, Kelly, and Heitman (1959). Heat loss measurements were made on 43 groups of hogs (groups consisted of 4 or 5 hogs) ranging in average weight from 20.4 to 172.4 kg in the Psychrometric Chamber under constant ambient temperature conditions. Management has been previously described (Bond *et al.*, 1959), and the chamber was modified to serve as an air calorimeter (Kelly, Heitman, and Morris, 1948; Bond, Kelly, and Heitman, 1952). The hogs were full-fed during the course of these experiments, and each experimental period lasted for 7 days. Calorimeter measurements were made of the heat removed from the Chamber during the last 2 or 3 days of each period.

RESULTS

Statistical treatment of the data permitted development of the following regression equation for prediction of total heat loss of swine under various combinations of body weight and ambient air temperature:

$$Y = 1.761 + 0.0357X_1 - 0.414X_2 + 0.148X_1^2 + 2.300X_2^2 - 0.563X_1X_2$$

where

Y = log total heat loss, kcal per hour per pig.
X_1 = log body weight, kg.
$100X_2$ = ambient air temperature, °C.

A nest of curves (Fig. 1) has been calculated for various weight animals at varying temperatures.

As observed by Brody (1945) the temperature range swine can stand on the cold side of thermoneutrality is greater than on the hot side. The nonsweating nature of

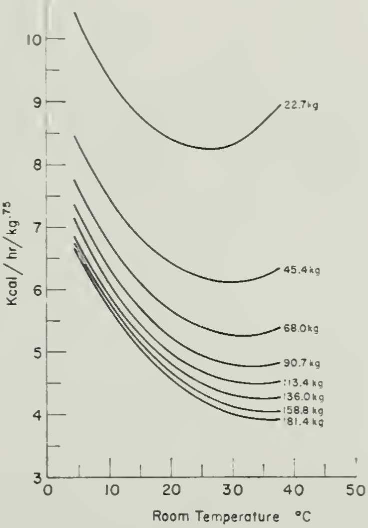

FIG. 1. Regression curves showing the relationship of animal weight $^{3/4}$, air temperature, and total heat loss of hogs

swine probably is related to this phenomenon. The curves previously observed (Bond *et al.*, 1959) were much flatter for large hogs than smaller ones (Brody, 1945). The curves presented herewith per unit of weight $^{3}/_{4}$ do not emphasize this characteristic which is probably related to thermal insulation and resistance to heat flow (Kleiber, 1961).

Though heat loss is greater per unit of weight or weight $^{3}/_{4}$ for smaller animals, total heat loss per animal is greater for larger animals (Bond *et al.*, 1959; Brody, 1945). The temperature at which heat loss reached a minimum varied from approximately 26.7° to 33.3° C for pigs varying in weight from 22.7 to 90.7 kg, respectively. Heavier hogs weighing from 136.1 to 181.4 kg failed to reach a minimum in heat production through the temperature range studied.

There is no distinct zone of thermoneutrality in these curves, and there are no inflection points to indicate the critical temperatures. For discussion, the minimum heat loss values, or points of thermoneutrality (Brody, 1945), will be used since attempts to extract zones of thermoneutrality are not possible:

Pig weight, kg	Thermoneutrality point, °C
22.7	26.7
45.4	29.4
90.7	33.3

The increase in the ambient air temperature with the increase in body weight was unexpected as well as was the magnitude of the temperatures. They are higher than the ambient temperatures found for maximum weight gain and change in an opposite direction with regard to body weight (Heitman *et al.*, 1958).

The ambient temperatures for minimum heat loss of fed hogs are higher than were reported for critical temperature of hogs under resting conditions (*ibid.*) and would be expected due to the calorigenic effect of feed (Kleiber, 1961). Since feed consumption and weight gain are both affected by ambient temperature (Heitman and Hughes, 1949), the effect of temperature on feed utilization cannot be predicted for various weight pigs. There is a positive correlation between feed consumed and weight gain (Headley, 1946; Magee, 1962), and it has been assumed that feed consumed will also be correlated to feed conversion so that the more feed consumed the less feed will be needed per unit of gain. Since faster growing pigs must be maintained fewer days, it is commonly believed that they will be more efficient in feed utilization. It has been indicated that swine restricted in feed (and therefore gaining more slowly) require less feed per unit of gain (Merkel *et al.*, 1958; Winters, Sierk, and Cummings, 1949). Magee (1962) has demonstrated, however, in pigs fed *ad libitum* that daily feed intake and desirable feed efficiency (gain per unit of feed) are negatively correlated. The data presented by the above workers would make it difficult to correlate average daily gain to feed per unit of gain to zone of thermoneutrality.

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DIE BEDEUTUNG DER TENDENZEN PHYSIOLOGISCHER MESSWERTE TEMPERATURBELASTETER GROSSTIERE ALS REAKTIONSMERKMALE

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Abstract — In evaluating the productive capacity of individual farm animals the ability of the animals to respond to the stress imposed on them by the meteorological elements is of primary importance. The present report deals with physiological responses of six milking cows to heat and cold stress, exemplified by the behaviour of the haematocrit, blood sugar concentration, total protein concentration of blood serum, and specific conductivity of the blood. Associations were found between the speed and intensity of the response on the one hand and the capacity for milk production on the other hand.

Zusammenfassung — Der Unsicherheitsfaktor, welcher den Schätzungen des individuellen Leistungsvermögens von Haustieren innewohnt, lässt nach neuen Wegen zu ihrer Bestimmung suchen. Eine ausschlagebende Rolle spielt hierbei das Reaktionsvermögen gegenüber meteorologischen Umweltfaktoren. Es wurden daher Untersuchungen an Milchkühen über das Verhalten einer grösseren Anzahl physiologischer Messwerte während und nach Wärme- und Kältebelastung durchgeführt. Am Beispiel von vier Messwertreihen (Haematokritwert, Blutzuckergehalt, Gesamteiweissgehalt des Blutserums, spezifische Leitfähigkeit des Blutes) von sechs Milchkühen unterschiedlicher Leistungsfähigkeit werden Parallelen zwischen individuellen Reaktionstendenzen, -geschwindigkeiten und -intensitäten sowie dem Leistungsvermögen demonstriert.

Résumé — Lors de l'évaluation des capacités de production des animaux domestiques considérés comme individus, leurs prédispositions à réagir à certaines tensions qui leur sont imposées par les éléments météorologiques est de première importance. En conséquence, on a procédé à des essais avec des vaches laitières exposées au froid et au chaud. On a en particulier examiné plusieurs grandeurs physiologiques. Sur la base de quatre séries (valeur de l'hématocrite, de la teneur en sucre du sang, taux total en protéine du sérum sangüin, conductibilité spécifique du sang) provenant de six vaches laitières de productivité différente, on tire des parallèles entre la vitesse et l'intensité des réactions individuelles ainsi qu'entre la production laitière de chacune d'elles.

EINLEITUNG

Die menschlichen Bemühungen um Leistungssteigerungen der Haustiere sind sehr alt und intensiv. Neben der unerläßlichen Verbesserung der Haltungsbedingungen war man bestrebt, Methoden zu entwickeln, welche es erlauben, schon möglichst frühzeitig am Individuum selbst festzustellen, ob die Entwicklung der Leistung des Tieres voraussichtlich den gewünschten Weg gehen werde oder nicht. Dazu gab das Zweckmäßigkeitsprinzip im Bauplan der Natur eine wesentliche Hilfe. Die danach zu erwartende gewisse Einheit von Habitus und Funktion ließ sich dahingehend auswerten, daß aus dem morphologischen Erscheinungsbild Schlüsse auf die Reaktionsfähigkeit des zu beurteilenden Individuums gezogen wurden. Diese Reaktionsfähigkeit macht es dem Organismus möglich, im ständigen Wechselspiel mit den Einflüssen der Umgebung rechtzeitig und im richtigen Maße diejenigen Regulationsmechanismen einzusetzen, welche das für einen optimalen Ablauf der Körperfunktionen notwendige Gleichgewicht erhalten.

Es ist sehr schwierig und zum Teil unmöglich, die Reaktionswege der einzelnen Reizbeantwortungen aufzuzeigen. Ein Faktor ragt dominierend aus der Fülle der Beeinflussungsmöglichkeiten heraus: die Lufttemperatur. Durch sie ist es möglich, den Warmblüterorganismus am ehesten und kräftigsten zum Einsatz seiner Regulationsmechanismen zu zwingen. Von der Temperatur ist anzunehmen, daß ihre Beherrschung durch den geringstmöglichen Energieaufwand eine positive Auswirkung auf das sonstige Leistungsvermögen des Körpers haben müßte.

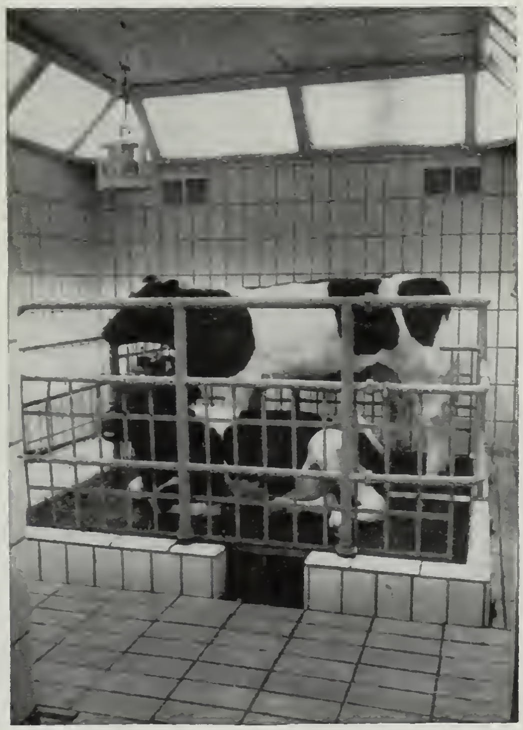

Abb. 1. Klimakammer, hier eingerichtet zur Aufnahme von zwei Großtieren

METHODIK

Wir haben Vorversuche an Kühen durchgeführt und in unserer Klimakammer für Großtiere (Abb. 1) in Reihenuntersuchungen Tiere jeweils Wärme- und Kältebelastungen ausgesetzt. Dabei konnten wir feststellen, daß es auf diesem Wege tatsächlich möglich ist, individuelle Reaktionsunterschiede festzustellen.

Drei Wochen lang wurden täglich zwei- bis fünfmal durch Punktion der Vena jugularis Blutproben entnommen und im Laboratorium elf Untersuchungsgängen (Haemoglobin, Haematokrit, Eosinophile Granulozyten, Osmotische Resistenz der Erythrozyten, Blutzucker, Blut-pH, Spezifische Leitfähigkeit, Gesamtserumeiweiß, Serumeiweißfraktionen (elektrophoretisch), Serum-NaCl, Serum-Alkalireserve) unterzogen. Jedes Morgen- und Abendgemelk lieferte eine Milchprobe, die jeweils acht Analysen durchlief (pH-Wert, spezifische Leitfähigkeit, Milcheiweißgehalt, Milchzuckergehalt, Soxhlet-Henkel-Wert, Milchchlorgehalt, spezifisches Gewicht, Milchfettgehalt, Milchmenge). Ausserdem wurden Herzschlagzahl/Min und Atemzugzahl/Min sowie Rektaltemperatur und Hauttemperatur am Widerrist gemessen.

Die erste Woche lief als reine Kontrollperiode ohne thermische Belastung ab. Am Anfang der zweiten Versuchswoche stand eine Wärmebelastung von 24 Stunden Dauer bei $+35°$ C ($=95°$ F) mit 27,0 g H_2O/m^3 Luft.

Der Rest der zweiten Woche diente dem Abklingen der angelaufenen Reaktionen. Am Beginn der dritten Woche stand eine achtstündige Kältebelastung bei $-8°$ C ($=17.6°$ F). Auch der Rest dieser Woche diente der Beobachtung des Abklingens der Reaktionen.

ERGEBNISSE

Aus unseren bisherigen Untersuchungen geht hervor, daß bei den meisten Meßwerten die Belastungsbeantwortung durch die leistungsstärkeren Individuen schneller und intensiver erfolgte als durch die Tiere mit niedrigerer Leistung.
Aus den obengenannten Blutanalysenwerten seien, stellvertretend für die Mehrzahl, einige herausgegriffen, welche besonders deutlich die unterschiedliche Reaktion von Tieren verschiedener Leistungen demonstrieren:

(1) Der Haematokritwert (Abb. 2) In der Wärmebelastung fanden wir zunächst einen Abfall des Anteils geformter Bestandteile im Blut mit darauffolgendem Wiederanstieg. Dieser letztere blieb während des Berichtszeitraumes, welcher bis 48 Stunden nach Belastungsende dauerte, bestehen, war aber schwächer ausgeprägt. Die Normalisierung ist also in dieser Zeit noch nicht abgeschlossen. Während das absolute Ausmaß der Verschiebungen keine sicheren Unterschiede zwischen leistungsstärkeren und leistungsschwächeren Tieren erkennen liess, war die Zeitspanne bis zum Erreichen des Minimalwertes bei den besseren Tieren mit durchschnittlich 3,3 Stunden erheblich kürzer als bei den schlechteren Tieren mit durchschnittlich 6 Stunden. Die Tendenzen und ihr kompensatorischer Ausgleich waren in der

Kältebelastung unterschiedlich, sodaß hierzu weitere Untersuchungsergebnisse abgewartet werden müssen.

(2) Die Tendenz des Blutzuckergehaltes (Abb. 3) war – im Gegensatz zur Kältebelastung – in der Wärmebelastung nicht einheitlich. Von den drei Tieren mit der höheren Leistung fielen die Werte von zwei Tieren kurz nach Belastungsbeginn,

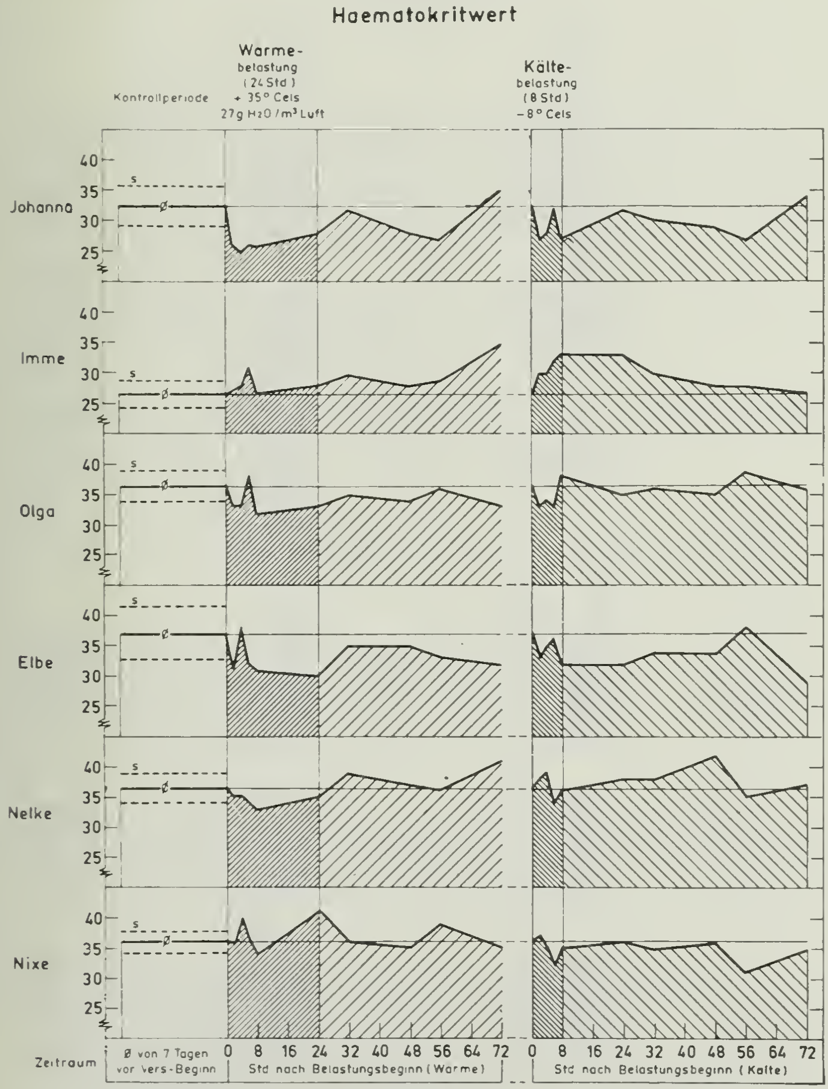

Abb. 2. Verlauf der Haematokritwerte

während bei dem dritten die Werte erheblich anstiegen. Die Überkompensation trat erst nach 32–56 Stunden ein und pendelte sich dann zum Normalwert ein. Bei den schlechteren Tieren reagierten zwei mit einem sehr starken Anstieg und eins mit einem ganz schwachen Abfall von 5,74% des Mittelwertes. Einheitlicher wurde das Bild in der Kältebelastung. Mit nur einer Ausnahme fanden wir zunächst einen

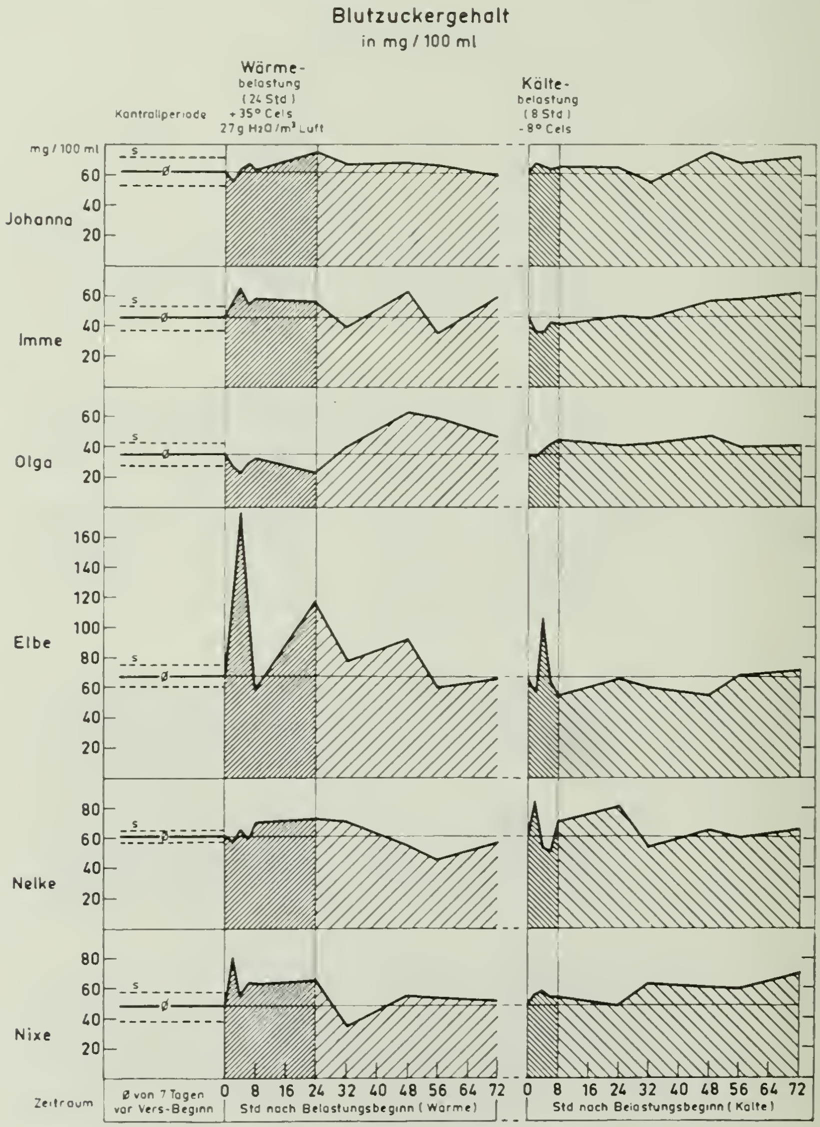

Abb. 3. Verlauf der Blutzuckerwerte

starken Anstieg des Blutzuckergehaltes um 10,88–56,14%, dem dann die schwächer ausgeprägte Hypoglykaemie folgte. Nur bei einem Individuum (IMME) erschien in kurzer Zeit die Hypoglykaemie, welche sich bis zur 72. Stunde nach Belastungsbeginn (=64. Stunde nach Belastungsende) zur Hyperglykaemie wandelte. We-

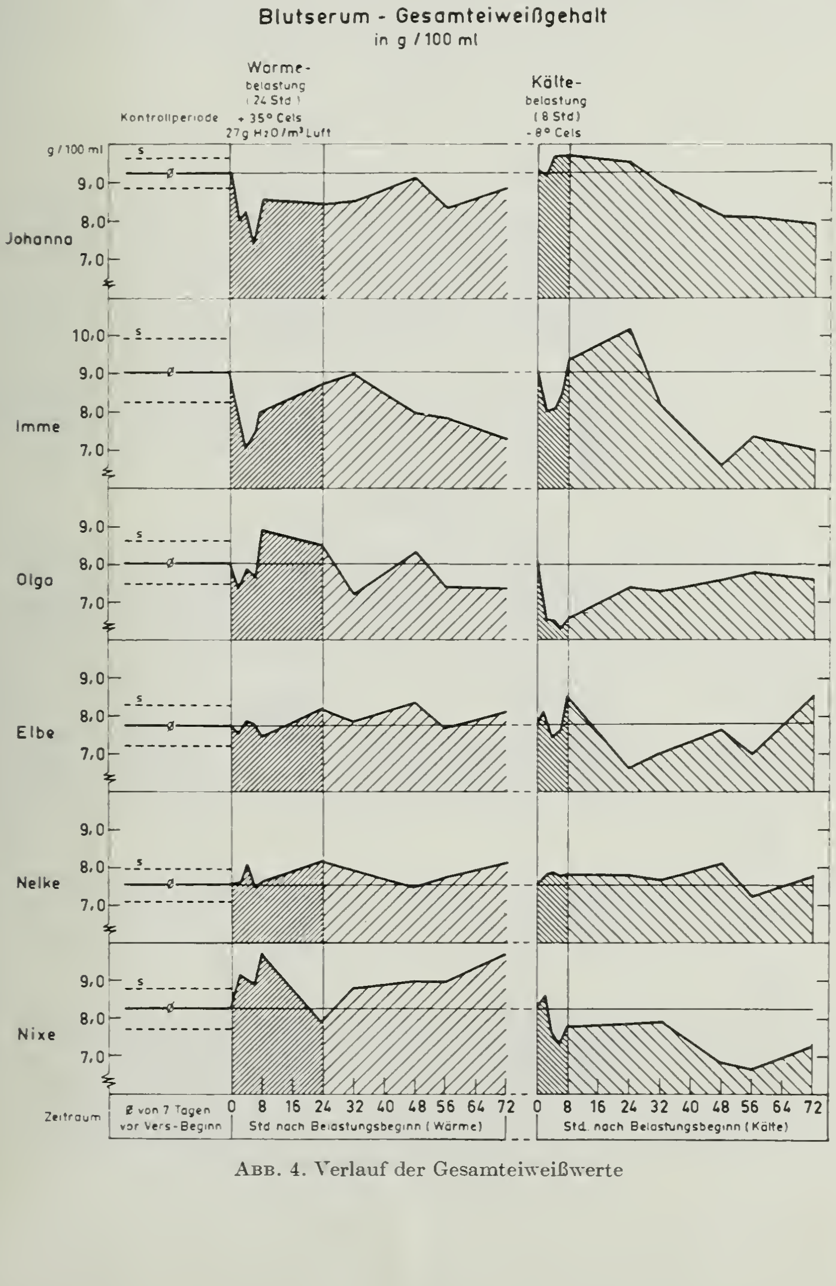

ABB. 4. Verlauf der Gesamteiweißwerte

gen des besonders starken Einflusses des Stoffwechsels und der Ernährung auf den Blutzuckergehalt war dieser Wert starken Schwankungen unterworfen. Es wird zahlreicher weiterer Untersuchungen bedürfen, um hier zu einem brauchbaren Einblick in die Verhältnisse während und nach thermischer Belastung zu kommen.

(3) Beim Gesamteiweißgehalt des Blutserums (Abb. 4) ergab sich daß die schlechteren Tiere mit einer teilweise erheblichen Verzögerung auf die Belastung,

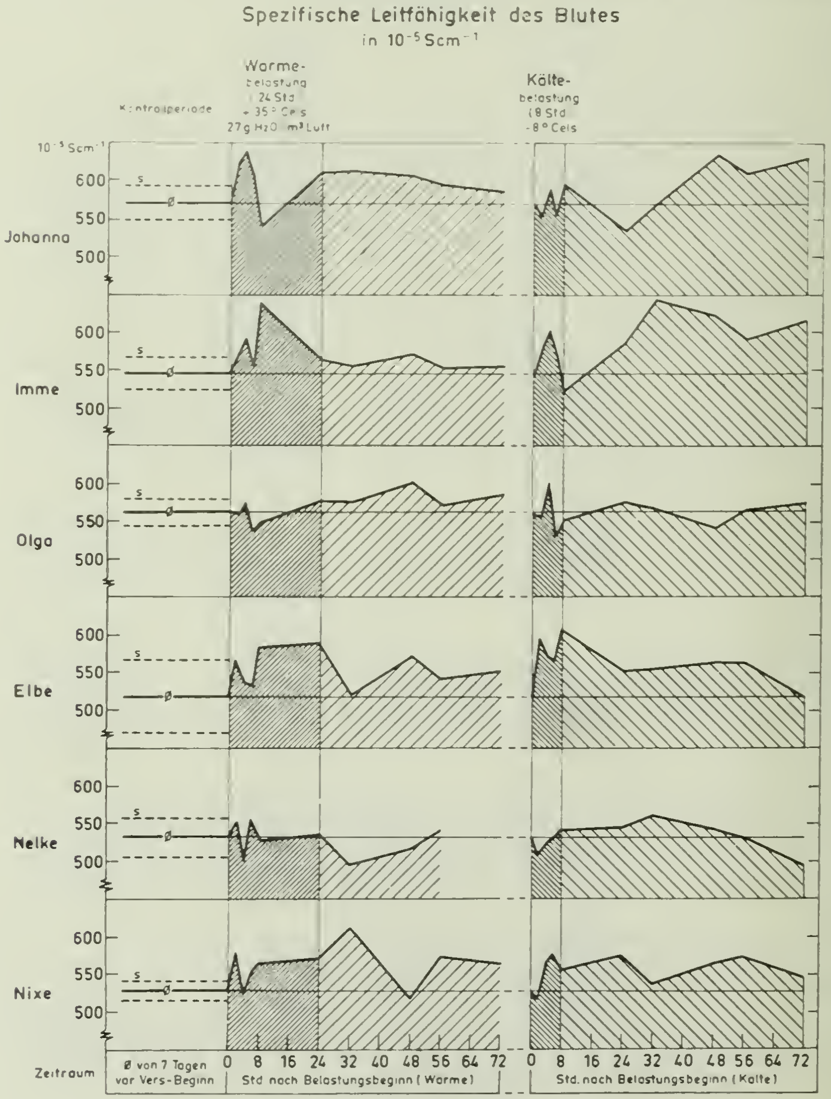

Abb. 5. Verlauf der Leitfähigkeitswerte

hier insbesondere auf die Kältebelastung, reagierten. Die in der Wärmebelastung auftretende Verminderung des Gesamteiweißgehaltes lag bei den besseren Tieren, welche zudem schneller reagieren (nach 4 Stunden), zwischen 8,06 und 21,71%, bei den schlechteren zwischen 0,53 und 4,23% des Mittelwertes. Außerdem lagen die Mittelwerte der Kontrollperiode bei den leistungsstärkeren Tieren um 12,02% höher als bei den Individuen mit geringerer Milchleistung.

In der Kältebelastung setzte sich die Tendenz einer schnelleren Reizbeantwortung durch die besseren Tiere fort, ohne aber in der Intensität die gleichen Unterschiede zu zeigen.

(4) Bei der Spezifischen Leitfähigkeit des Blutes (Abb. 5) fiel besonders auf, daß unsere besseren Individuen zwar träger auf Belastungen reagierten, dann allerdings stärkere Verschiebungen zeigten. Die Tiere Johanna, Imme und Olga zeigten erst nach 4–8 Stunden Wärmebelastung wesentliche Abweichungen. Diese erreichten dann aber auch 7,13–17,11% des Mittelwertes.

Die Reaktionen der leistungsschwächeren Tiere Elbe, Nelke und Nixe waren bereits nach zwei Stunden deutlich festzustellen. Sie lagen zwischen 3,99 und 9,26% der Mittelwerte der Normalzeiten. Außerdem ist zu erwähnen, daß bei diesem hier vorgestellten Material die leistungsstärkeren Tiere allgemein um 6,5% höhere Leitfähigkeitswerte zeigten als die leistungsschwächeren.

DISKUSSION

In solcher oder ähnlicher Weise verliefen die Belastungsreaktionen bei fast allen von uns geprüften physiologischen Meßgrößen.

Die hier vorgetragenen Beobachtungen stammen aus einer ersten Sichtung des bisher vorliegenden Materials von zur Zeit 26 Kühen, wobei wir, am Maßstab ihrer ersten Laktationsleistungen gemessen, die bisher besten drei Tiere den schlechtesten drei Tieren gegenüberstellten.

Wir führen diese Untersuchungen fort und werden bestrebt sein, auch andere Rassen und Haltungsformen auf ihre Reaktionsfähigkeit gegenüber thermischen Belastungen zu prüfen.

THE MEASUREMENT OF RESPIRATORY GASEOUS EXCHANGE IN CATTLE USING MASK METHODS

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Abstract – Experiments on calves standing in a thermoneutral environment have shown that the variability of heat production measurements using a mask method may be kept as low as 6–7 per cent, provided the measurements are made over periods of not less than 2 min. Extension of the measuring period beyond this time results in no appreciable improvement in repeatability. The limitations of the mask method and the precautions that need to be taken in its application to cattle are discussed. In view of the shortness of the sampling period necessary for heat production measurements, it appears that a mask method involving total collection of respiratory gases in some form of Douglas bag would be of practical use in the field.

Zusammenfassung – Versuche mit Kälbern in einer thermoneutralen Umgebung haben gezeigt, dass die Variabilität der Messung der Wärmebildung mit Hilfe einer Maskenmethode unterhalb von 6 bis 7% liegt, sofern eine Messdauer von 2 Minuten nicht unterschritten wird. Eine Ausdehnung der Messdauer auf mehr als 2 Minuten hat keine wesentliche Erhöhung der Reproduzierbarheit zur Folge. Die Begrenztheit der Maskenmethode und die speziellen Massnahmen, die bei der Verwendung beim Rind berücksichtigt werden müssen, werden besprochen. Die Methode dürfte sich für Untersuchungen im Freien eignen, da infolge der Kürze der Messdauer die Gasproben in einem relativ kleinen Douglas Sack aufgefangen werden könnten.

Résumé – Des veaux tenus dans un milieu thermiquement neutre ont montré que la variabilité des mesures de la production calorifique, mesures faites avec un masque respiratoire, restaient au-dessous de 5 à 7 pour cent à condition de procéder aux essais durant plus de 2 minutes. Si l'on prolonge les mesures au-delà de 2 minutes, on n'en augmente pas sensiblement la précision. On discute ensuite les limites de la méthode du masque respiratoire chez les bovidés et les précautions spéciales qui y sont nécessaires. Cette méthode peut également être utilisée pour des essais en plein air, car, en raison de la courte durée des mesures, les échantillons de gaz peuvent être recueillis dans un sac de Douglas relativement petit.

Many studies of the effects of climate on animals are restricted in scope by lack of a simple method of measuring heat production. Use of a mask may be criticized on the grounds that it disturbs the animal, a defect that cannot be entirely avoided even by the most careful design of valves and elimination of dead space. Nevertheless the mask method is the only means of measuring the heat production of the intact animal in the field. The alternatives are tracheostomy, which achieves a slightly different objective since gases formed in the rumen are not collected, or the enclosure of the entire animal in a respiration chamber. This paper deals with an investigation into the practical techniques of employing the mask method.

MATERIALS AND METHODS

The apparatus used is shown in Figs. 1 and 2. The mask is made of metal and rubber, and is sealed onto the muzzle by means of an inflatable tube round the top opening. The valves are designed to be as light as possible and may be held fully

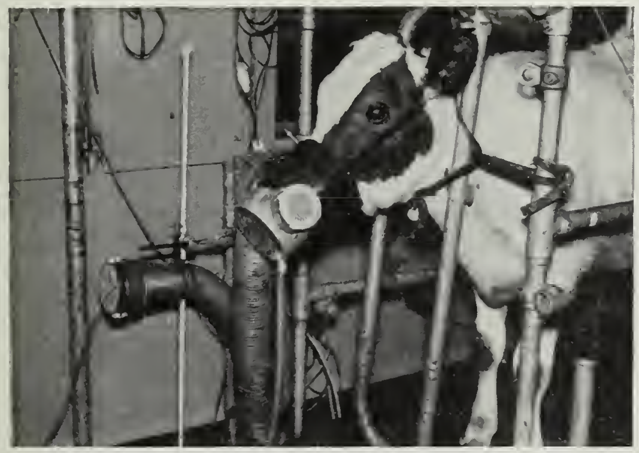

FIG. 1. Photograph of an animal wearing the mask

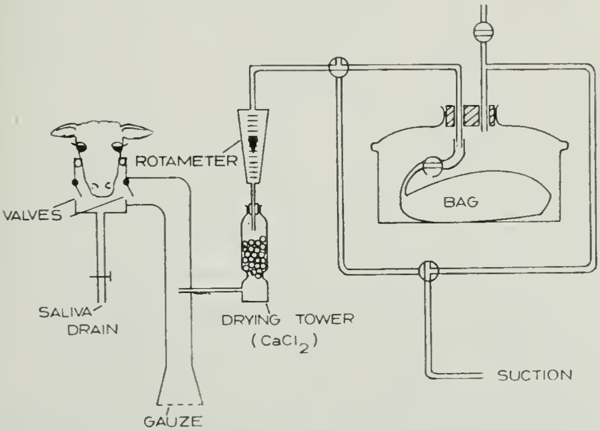

FIG. 2. Diagram of mask and associated apparatus

open by a pressure of about 1.5 mm water. The respiratory volume is measured by a screen flowmeter or pneumotachometer designed by Nisbet (1956), the sensing gauze being situated at the exhaust end of a piece of flexible tubing. The gas sample is drawn into a butyl sampling bag by evacuating a vessel which contains the bag. The network of tubes and taps is arranged to simplify the process of washing out the bag before gas sampling.

Three 4 to 6-month-old calves were used in an experiment to determine the repeatability of heat production measurements by this method. The animals soon became accustomed to wearing the mask and after a week's training they were frequently seen ruminating while wearing it. Each day at 09 : 00 h, one animal entered a climatic room, controlled at 20° C, and ten measurements were made at fixed times throughout the morning. The duration of the measurement, i.e. the time interval over which the volume was measured and throughout which the sample was collected, was held fixed each day. On separate days, however, sampling durations of 1, 2, 4, 8 and 16 min were employed. Two runs, each consisting of five daily exposures with the mask and one control exposure without the mask were made with each animal. The measurements from an earlier pilot run on an older animal were also included in the analysis of the results. The animals were normally fed twice daily but on days when measurements were to be made the morning feed was withheld until after the experiment.

RESULTS

In order to determine the effects of the mask on respiratory exchange the only relevant quantity that could be measured both in the presence and absence of the mask was the respiratory rate. One of the animals had a respiratory rate 60 per cent higher on days when the mask was worn than on days when it was not. For the others, however, the difference was less than 10 per cent and for one of the animals, the respiratory rate was lower when the mask was worn. The mask thus had a variable effect on respiratory rate.

The variation of the heat production, respiratory ventilation and respiratory rate with time of day is shown in Fig. 3. Heat production was significantly lower for the first three measurements each day than for the remainder, but the difference was only of the order of 5 per cent. Respiratory ventilation and respiratory rate also rose, following the start of the exposure, to reach maximal levels at about the time of the fifth or sixth sample, after which they declined slowly. That these trends are not primarily responses due to wearing the mask is suggested by the fact that respiratory rate showed similar trends in the control experiments with no mask, although, as just described, respiratory rate was on average higher (by 13 per cent) when the mask was worn than when it was not. The relatively steady mean level of heat production during the morning, especially for the last seven samples, justifies examination of the variability of the results within each day as a measure of the repeatability of the method.

One of the animals habitually lay down for part of the time. Table 1 shows the mean differences in heat production, respiratory rate and respiratory ventilation

Table 1. The Effects due to the Animal Lying Down (based on 56 Measurements on one Animal in the Standing Position and 30 in the Lying Position)

	Standing level	Change due to lying down and standard error	% Change
Heat production (kcal/hr)	189.1	-12.3 ± 4.4	-6.5
Respiratory ventilation (l./min)	22.3	-2.0 ± 0.6	-8.8
Respiratory rate/min	28.0	$+2.9$	$+10.2$

of this animal when lying compared with the standing levels. Heat production and respiratory ventilation were both lower when the animal was lying, but respiratory rate was higher. The reduction in heat production due to the animal lying was 6.5 ($\pm$2.8 SE) per cent; in an earlier series of measurements on another of these same animals the reduction was 10.3 ($\pm$2.3 SE) per cent.

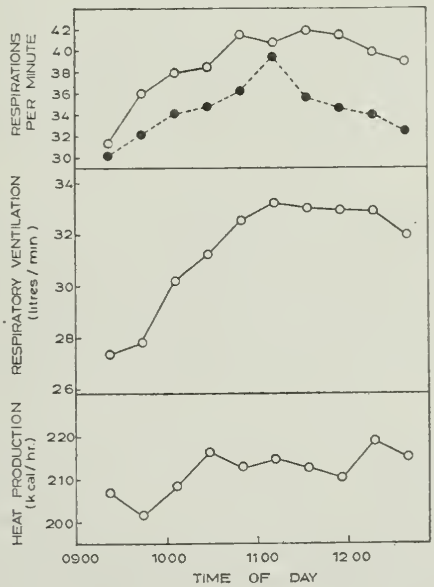

FIG. 3. Variation with time of day of heat production, respiratory ventilation and respiratory rate

The average variability of the measurements within each day, excluding variations due to changes of posture, is shown in Fig. 4 for each of the five rates of sampling used, i.e. for each duration of measurement. The variability of the heat production measurements was not appreciably increased by shortening the sampling period until a gas collection lasting only 1 min was employed. The variability of the respiratory ventilation measurements expressed as a percentage was in all

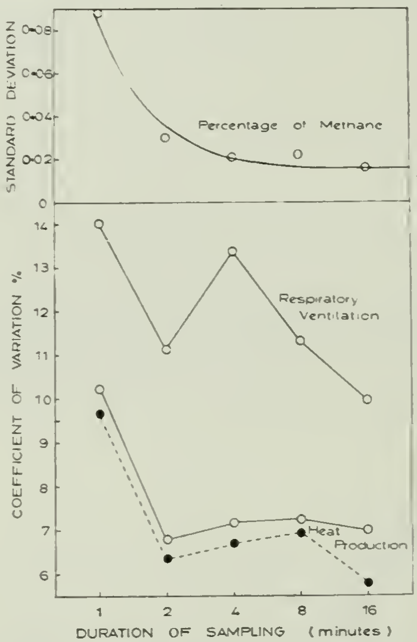

FIG. 4. Showing how the variability between successive measurements, for an animal in an unchanged posture, was reduced as the duration of the sampling period was increased. The second curve (● – – – ●) for the coefficient of variation of heat production is based on the measurements excluding the data from the first three samples each day

instances greater than the percentage variability of the heat production measurements; often it was twice as great. Since heat production was calculated from the product of respiratory ventilation and a factor which combined the changes in concentration of respired gases it follows that variations in respiratory ventilation must have been accompanied by compensatory variations in gas concentrations. Despite the minute-to-minute changes that occurred in respiratory activity the overall rate of gaseous exchange was remarkably steady. These facts emphasise the extreme importance in mask determinations of ensuring that the gas sample is collected throughout the full period during which respiratory ventilation is measured. The broken curve (Fig. 4) denotes the variability of heat production calculated from all the measurements except for the first three each day; omitting the first three measurements results in a lower overall variability but the effect of altering the duration of sampling is the same.

The variability of the percentage of methane in separate samples of expired air reached a minimum level only when the sampling duration was increased to 4 min. The imperfect sampling of methane was not, however, of great importance since under the conditions of the experiments the influence of the methane factor on the overall calculated value of heat production was small. For measurements of heat production following closely after feeding variations in methane output may well be of greater importance and sampling might have to be prolonged.

In earlier experiments (McLean, 1963) it was found that due to rebreathing of previously expired air the respiratory moisture loss was considerably reduced by the presence of the mask, even though the dead space was kept as small as possible. Rebreathing of previously expired carbon dioxide must also occur and some increase in blood P_{CO_2} may be expected due to the presence of the mask. When a mask is put on an animal, some time must elapse before the concentrations of the respiratory gases attain their new equilibria. For this reason and to avoid disturbing the animal by excessive handling we believe that the mask should, whenever possible, be worn throughout the experimental period and not be put on and taken off for each measurement. We always allow at least 15 min after putting on the mask before making the first measurement.

The experiments that have been described here suggest that once the mask has been worn for some time, measurements of heat production repeatable to within 7 per cent may be obtained in periods as short as 2 min. This means that for measurements in the field the screen flowmeter and sampling apparatus that we have used could be replaced by some form of Douglas bag. For 2-min collections of expired air the bags would not have to be excessively large.

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WATER EXCHATGE OF CATTLE UNDER HEAT STRESS

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Abstract – Cattle adapt well to direct effects of high environmental temperature. The most important adjustments are those in which water plays a role. Cattle acclimatized to temperature of 32° C drink 2–4 times more water than would animals kept at 2° to 10° C. Water consumption is highly correlated with body temperature. In a hot environment there is little change in faecal water, but there are significant increases in urine volume (25 per cent), evaporation from the respiratory tract (54 per cent) and evaporation from the skin (177 per cent). The increase in the skin evaporation is mainly due to sweating. The magnitude of the individual variation in water consumption and water output suggest genetic differences; these should be considered.

Zusammenfassung – Das Rind besitzt ein gutes Anpassungsvermögen gegenüber den direkten Auswirkungen hoher Umgebungstemperaturen. Die wichtigsten Anpassungsvorgänge sind diejenigen, bei welchen Wasser eine Rolle spielt. Die Wasseraufnahme von Rindern, die an eine Umgebung von 32° C akklimatisiert sind, ist 2–4 mal grösser als diejenige von Kontrolltieren, die bei 2° – 10° C gehalten werden. Zwischen Wasseraufnahme und Körpertemperatur besteht eine hohe Korrelation (0.7). In der Hitze ändert sich die Wasserabgabe durch den Kot nur geringfügig, dagegen tritt eine signifikante Erhöhung der Urinmenge (25%), der Atmungsverdunstung (54%) und der Hautverdunstung (177%) ein. Die erhöhte Hautverdunstung erfolgt hauptsächlich über die Schweissdrüsen. Die Grösse der individuellen Variation in der Aufnahme und Abgabe von Wasser deutet auf genetisch bedingte Unterschiede hin; diese sollten berücksichtigt werden.

Résumé – Les bovidés s'adaptent facilement aux effets directs de hautes températures ambiantes. Les processus d'adaptation les plus importants sont ceux où l'eau joue un rôle prépondérent. Un bovin acclimaté à une chaleur de 32° C boit 2 à 4 fois plus qu'une bête de contrôle tenue à 2 à 10° C. On note une haute corrélation entre les quantités d'eau absorbées et la température du corps ($r = 0{,}7$). Les quantités d'eau éliminées par les déjections ne varient que peu sous l'effet de la chaleur. On constate par contre une forte augmentation de l'urine (25 pour cent), de l'évaporation respiratoire (54 pour cent) et de l'évaporation cutanée (177 pour cent). L'augmentation de l'évaporation cutanée est principalement due à l'activité des glandes sudoripares. L'amplitude des variations individuelles montre qu'il existe des différences génétiques. Il est donc indispensable d'en tenir compte.

CATTLE producers have long recognized the value of free access to water as essential to good performance of their animals under hot conditions and that water intake is associated with dry matter consumption. However, an appreciation of how cattle utilize water in thermo-regulation is only now emerging.

The purpose of this paper is to examine some of the more recent findings on the role of water in the adaptation of cattle to heat stress from the standpoint of free water intake, means of water loss, and some of the factors influencing the rate of water loss.

WATER CONSUMPTION

A number of reports, including Thompson *et al.* (1949); Ragsdale *et al.* (1949 and 1951); Weldy (1962); Winchester and Morris (1956), and Mullick *et al.* (1952), have shown that cattle increase water intake as air temperature increases with the major increase occurring above 80° F. The frequency of drinks also increases 3 to 4 times at 100° F over that at 40° F. Ragsdale *et al.* (1949) report no significant change in consumption from 4 to 80° F but intake rises thereafter with some decline at 95° F. These authors conclude that the critical temperature for water intake of lactating Jerseys and Holsteins is 80° F and that at temperatures below this point water consumption paralleled feed consumption. The critical level varies, however, with breed and stage of lactation, viz 85° F for lactating Brown Swiss and 90° for dry Brahman.

Level of feed intake and type of ration also influence the amount of water consumed. Ritzman and Benedict (1924) found that steers on a high-protein ration drank 26 per cent more than on a low-protein feed, while Breidenstein, *et al.* (1960) report that cows on high roughage consumed significantly more water. If such a relationship exists then the decrease in water consumption at 95° F reported by Ragsdale and co-workers could have been mainly an indirect effect, through lowered feed intake.

The Missouri Laboratory (Thompson *et al.*, 1954; Brody *et al*, 1954) reports no appreciable affect of changing the rate of air movement from 0.4 to 8 mph on water consumption at 18, 50, 65 and 80° F temperatures, and changing the radiation from 5 to 180 B.t.u./ft^2/hr had no effect on intake at 45°; but the higher radiation level had a significant effect at 70° and 80° F.

None of the studies discussed thus far have been of sufficient duration to permit the animals to become adjusted to the temperature conditions. Recent studies at Beltsville, under prolonged heat stress — 90° F for 16–30 weeks — made to determine some of the physiological changes involved in adaptation to heat, showed that level of intake undergoes quite a change during the adjustment period (Figs. 1 and 2). The tests were initiated in late December after the animals had become adjusted to winter conditions. A high energy pelleted ration was used to minimize depression of feed intake. In the Shorthorns there were no feed refusals and less than 3 per cent in the Herefords during the test periods. Figures 1 and 2 show mean weekly changes in rectal temperature, water consumption and hair coat depth for the Shorthorns and Herefords, respectively. Without change in the ambient temperature conditions, both groups of animals readjusted their body temperature levels after 14 weeks in the Shorthorns (Fig. 1) and 11 weeks in the Herefords

(Fig. 2). Water consumption increased markedly in the early weeks and remained 2 or more times the initial level after the heat balance had been restored. Water intake and body temperature were highly correlated, 0.69 for Shorthorns and 0.72 for the Herefords. In the Shorthorn study, hair coat depth and water consumption were associated with 70 per cent of the variation in rectal temperature while re-

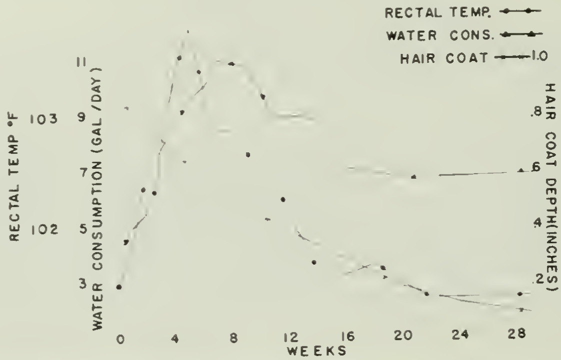

Fig. 1. Means of body temperature, water consumption and hair coat depth of Shorthorns exposed to a constant 90° F temperature with 22 mm Hg vapor pressure for 30 weeks

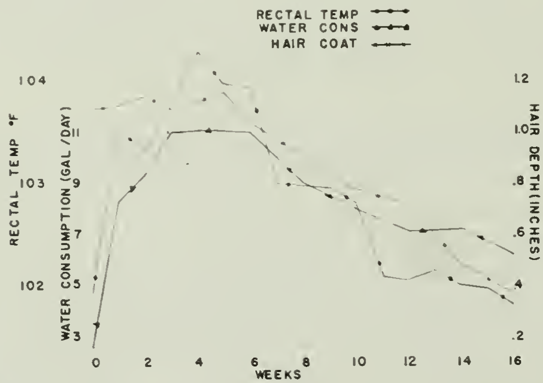

Fig. 2. Means of body temperature, water consumption and hair coat depth of Herefords exposed to a constant 90° F temperature with 22 mm Hg vapor pressure for 16 weeks

spiration rate accounted for less than 5 per cent. Water intake also showed significant correlations with blood ketones, 0.33 to 0.45, and with rumen fatty acid levels, −0.37 to −0.52. Correlations with blood cell volume and glucose, however, were near zero. Results from the Missouri Laboratory (Johnson *et al.*, 1958 and 1960) with dairy and beef heifers reared at 50° to 80° F temperatures are in agreement as the 80° reared heifers consumed an average of 73 per cent more water than the 50° group. These observations indicate that free water intake is closely associated with heat balance and should be further evaluated as a possible means of identifying animals best suited for high temperature conditions. The wide variation among individuals suggests a genetic relationship.

WATER LOSS

If it is accepted that on the average cattle increase their water intake 100% or more from 70 to 90° F, then the question logically arises: how is the extra water removed from the body? Weldy (1963) working with non-lactating Holsteins, fed a high energy ration at the rate of 15 per cent above maintenance for two week periods of alternating 70° and 90° temperatures, reported that water intake increased an average of 110 per cent by the second week at 90°. Water loss through the faeces showed little change the first week at 90° but decreased slightly the 2nd week (Table 1). By the end of the 2nd week urine volume had increased 25 per cent above the 70° level, respiratory evaporative losses were up 54 per cent, and salivation increased. The most marked change, however, was in surface evaporation, which increased an average of 177 per cent. Although the number of animals involved (12) was too small for the results to be conclusive, indications are that the major use made of the higher water intake was in surface evaporative cooling.

Table 1. Mean Water Loss (lb/24hr) by Non-lactating Holstein Cows at 70° and One and Two Weeks at 90° F. (Data from Weldy and McDowell, 1962)

Air temp.	Faeces	Urine	Saliva	Respiratory	Surface
70	28.6	25.8	0.0	16.7	23.3
90	29.5	30.4	4.7	24.4	57.8
90	21.6	32.4	5.3	25.8	64.6

Water lost through Faeces

Air temperatures 80° F and above usually cause a suppression in feed intake; thus any significant change in moisture loss through the faeces would be by change in the water content of the faeces. Preliminary evidence (Weldy, 1963) indicates some slight change by individuals but generally the water content of the faeces remains in the range of 75 to 85 per cent irrespective of level of air or body temperature.

Urine

Schmidt-Nielsen (1958) has amply demonstrated that certain animals have a remarkable capability of concentrating their urine when faced with a shortage of water. While this facility is most marked in the kangaroo rat, it is shared by the camel which has a further advantage in times of water deprivation, in that it can conserve some of the nitrogenous waste normally excreted in the urine and utilize it to offset lack of food nitrogen. Merino sheep also seem capable of tolerating a similar water deprivation (Macfarlane *et al.*, 1956). Such capabilities have not been demonstrated to any extent in cattle. In general there is an increase in urine output with rising temperature, but the rate varies quite widely between individuals. For example, Thompson *et al.* (1949) reported that one Holstein showed a marked decrease in urine output at 100° F while a Jersey increased volume 5 times that of her 70° level. Similar variations have been observed with sheep kept at 85° and 95° F. (Kawashti, 1963). Those animals showing diuresis had lower body temperatures but the advantages have not been fully evaluated. It would appear that most cattle show a moderate increase with rising temperature (Table 1); thus making only a modest use of this avenue of heat loss.

Salivation

The water loss through copious salivation is a very inefficient means of promoting heat loss. The amount of salivation varies quite widely and is largely dependent on the type of breathing. Observations at the Beltsville laboratory indicates "open mouth" breathers show the poorest tolerance to heat; hence, high levels of salivation may aid in identification of "poor doers".

Respiratory Evaporation

The volume of air respired per minute by cattle under high temperatures may increase fivefold or more over temperate conditions. With the expired air nearly saturated this is a means of evaporating significant amounts of water as shown in Table 2. As indicated by the data, respiratory vaporization rate is a function of several interrelated factors including environmental temperature, metabolic rate, stage of lactation (lactating vs. dry) and age (heifers vs. cows). It is also a function of pulmonary ventilation rate (Kibler and Brody, 1952; McDowell *et al.*, 1953). The rate (g/m^2 hr) appears to be similar among European breeds and significantly greater than for Brahman (Table 2) and Zebu-European crosses (Johnson *et al.*, 1958 and McDowell *et al.*, 1953). The reason for the differences between breed types is not clear but metabolic rate, pulmonary ventilation rate, and surface evaporation are factors.

Weldy and McDowell (1962) found significant differences in rate between 70° and one week at 90° F (Table 2) but no difference between the first and second

Table 2. Respiratory Evaporative Losses (g/m^2 hr) at Various Air Temperatures for Different Breeds

Air temp.	Jersey* Lact.	Brown Swiss*		Brahman*			Holstein		
		Lact.	Heifers	Lact.	Dry	Heifers	Lact.*	Dry†	Dry‡
50	20	26	13	12	10	7	27		
60	23	26	15	12	10	10	31		
70	27	30	16	15	12	8	30		49
80	35	39	18	14	13	13	41	37	
90	44	48	34	14	14	17	45	52	66
95	51	45	39	22	—	20	49	54	
100	38	55	51	26	21	27	42	53	

*Kibler and Brody (1950b, 1952);
†Barrada (1957);
‡Weldy and McDowell (1962).

Table 3. Percent of Total Vaporization Loss through the Respiratory Tract at Different Air Temperatures for Different Breeds

Air temp.	Jersey* Lact.	Swiss* Lact.	Brahman* dry	Holstein		Dry†	Dry‡
				Lact.*	Dry+		
50	36	39	23	40			
60	26	31	24	33			
70	22	22	29	20		42	33
80	21	23	27	22	26		
90	23	27	16	25	23	30	22
95	29	26	—	27	25		
100	24	29	17	21	26		

*Kibler and Brody (1950b, 1952); +Barrada (1957); †Weldy and McDowell (1962) ‡Yeck 1960).

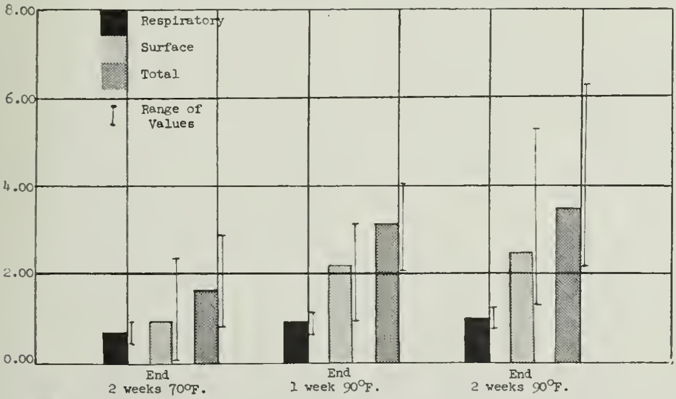

FIG. 3. Means and range of heat dissipation (therms/m^2 24 hr) for non-lactating Holsteins at 70° and 90° F. (Data from Weldy and McDowell, 1962).

week at 90° indicating there is a rather definite ceiling on respiratory evaporative losses (66 and 69 g/m^2 hr at one and two weeks respectively). Although respiratory losses increase with increasing temperature its proportion of the total shows little change (Table 3). Thus indications are that while both respiratory and surface evaporative losses increase with rising air temperatures, surface does so to a much greater extent. Also animal differences in rate of respiratory losses show much less variation than for surface (Fig. 3).

Surface Evaporation

When it comes to evaporative cooling from the body surface, we have a quiet, unobtrusive, largely ignored process which is proving to be a most important avenue of heat loss by cattle exposed to heat (Table 4). The major point of controversy is in the means whereby the water gets to the skin surface. That surface evaporation is more associated with activity of the sweat glands than with transudation of water through the skin is indicated by: (a) the presence of sweat glands widely distributed over the surface (Findlay and Yang, 1950; Dowling, 1955; Nay, 1959; Hafez *et al.*, 1955); (b) the marked reduction of evaporation by treatments known to affect sweat glands (Table 5); (c) the magnitude of the evaporation rate in most cattle examined (Tennenbaum, 1962; Kibler and Brody, 1950; Barrada, 1957; Weldy and McDowell, 1962; Taneja, 1959a; Robinson and Klemm, 1953); (d) the step increase in evaporation with increased heat load, Table 4; and (e) the appearance of wetness and even droplets on the skin (Schneider, 1949; Ferguson and Dowling, 1955; McDowell, 1963). The only serious objection to acknowledging the primary role of the sweat glands is the problem of obtaining reactions on starch paper from skin treated with iodine. This can possibly be explained by the way the moisture from the glands emerges in close association with the sebaceous secretion.

The within-cow correlation between surface evaporation and dry bulb temperature is high (0.76) and there is also a significant negative relationship (−0.47)

Table 4. Surface Evaporative Losses (g/m^2 hr) at Various Air Temperatures for Different Breeds

Air temp.	Jersey Lact.*	Brown Swiss* Lact.	Brahman*		Holstein		Dry†
			Lact.	Dry	Lact.*	Dry$^+$	
50	36	41	52	34	40		
60	64	57	57	31	64		
70	95	103	70	29	124		69
80	133	128	84	35	143	68	
90	138	128	154	73	133	127	155
95	123	128	156	—	134	136	
100	121	159	127	103	161	151	

*Kibler and Brody (1950b, 1952); $^+$Barrada (1957); †Weldy and McDowell (1962).

Table 5. Moisture Evaporation in 5 min from 10 cm² of Normal Skin and Skin with Sweat Glands Inactivated on a Red Sindhi Bull and a Dry Mature Holstein cow, taken between the Second and Fourth Hour of Exposure to 105° F and 34 mm Hg Vapor Pressure (Data from McDowell et al., 1961)

Time after treatment days	Untreated		Treated*	
	Forechest mg	Paunch mg	Forechest mg	Paunch mg
	Red Sindhi bull			
Experiment 1				
5	29.8	31.7	5.9	7.0
10	27.6	25.4	3.6	10.5
15	32.1	31.6	13.7	11.6
Experiment 2				
7	41.7	35.9	9.7	8.0
15	34.7	26.1	15.8	6.0
28	43.5	35.3	28.1	11.7
72	35.5	33.7	33.4	34.4
	Holstein cow			
4	29.5	—	13.0	14.0
5	29.5	—	10.0	12.0
6	31.6	—	12.5	13.0

* Three treatments of 10 min duration made on alternate days using 1.0 M amp/cm² current flow.

between surface evaporation and humidity (McDowell *et al.*, 1961). In studies at Beltsville we have found that dry bulb temperature and relative humidity accounted for 60 per cent of the variation in surface evaporation. Also rectal temperature is highly correlated with surface evaporation (0.66). Tennenbaum (1962) working with Friesians under field conditions in Israel reports that evaporation is probably more a function of skin temperature than of body or air temperature.

The cooling effect will be reduced by the thickness of the insulating layer of air formed by the hair coat; hence, a short smooth hair coat affords an advantage. McDowell (1963) found a significant negative correlation (−0.45) between hair coat depth and rate of surface evaporation. Tennenbaum (1962) found that losses from black areas on Friesians were higher than for white areas under direct sun but there was no difference under shade.

Studies in the Beltsville laboratory (McDowell *et al.*, 1961), have shown rather conclusively that rate of surface evaporation varies between different body areas with the rate from the trunk being uniformly higher than for the appendages. From our observations it is also apparent that once thermo-equilibrium is reached, evaporation rate is quite uniform for periods of at least $2^1/_2$ hr.

Breed differences (Ferguson and Dowling, 1955) as well as variation within breeds appear important (McDowell *et al.*, 1961) but which is the more important has not been determined. If we assume the sweat glands are the major contributor, then a higher density should be advantageous in which case the Zebu breeds would probably excell. The within breed variation among European breeds reported by Dowling (1955); McDowell *et al.* (1961); Weldy and McDowell (1962), suggest that individual variation is more important than breed. Weldy (1962) reports a range of 7.6–33.0 Therms/cow/day loss by non-lactating Holsteins at 90° F (Fig. 3). Such variations indicate a possible genetic relationship that should be evaluated. Based on limited observations in the field, Berman and Volcani (1961) report a heritability estimate for sweating in cattle of 0.37 which is encouraging.

As to the controlling mechanism of the sweat glands in cattle, we are not sure. One very limited study made by Taneja (1959b) suggests that their invervation is adrenergic. This is another point that needs further investigation.

Present evidence shows that many factors are involved in the progressive adaptation of cattle to heat stress; such as: (a) increased ease of heat loss; (b) decreased metabolic rate; (c) changes in the sensitivity of the heat regulating mechanism; and (d) increased toleration of either an elevated body temperature or some other consequence of the stress. Most of these mechanisms serve directly or indirectly to facilitate heat loss. Since evaporation of water from the body surface is the most efficient means for dissipating heat, much more attention should be given to the understanding of the processes involved as well as the genetic relationship. For an animal to make full use of surface evaporation, it must have the water available; therefore, means of increasing water consumption also warrant consideration.

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FACTEURS CLIMATIQUES ET BESOINS EN EAU CHEZ LES ANIMAUX DOMESTIQUES EN ZONE TROPICALE

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Abstract – A comparison of the water requirements of N'Dama cattle *(Bos Taurus)* and Zebu cattle *(Bos Indicus)* made under tropical conditions in Mali revealed that at environmental temperatures close to body temperature the depressing effect of high humidity was more pronounced in the Zebus than in the N'Damas. The Zebus were thought to be better suited for hot-dry regions, the N'Damas for hot-humid regions.

Zusammenfassung – Ein Vergleich des Wasserbedarfs von N'Dama Rindern *(Bos Taurus)* und Zebu Rindern *(Bos Indicus)* im tropischen Mali zeigte, dass bei Umgebungstemperaturen, die sich der Körpertemperatur nähern, die herabsetzende Wirkung hoher Luftfeuchtigkeit bei den Zebus stärker in Erscheinung trat als bei den N'Damas. Die Zebus schienen besser geeignet zu sein für heiss-trockene, die N'Damas für heiss-feuchte Gebiete.

Résumé – On a comparé les besoins en eau des boeufs N'Dama *(Bos Taurus)* et des Zébus *(Bos Indicus)* au Mali, c'est à dire en conditions tropicales. On a ainsi pu démontrer que la diminution du besoin d'eau provoquée par la forte humidité était plus prononcée pour les zébus que pour les boeufs N'Dama quand la température ambiante se rapprochait de la température du corps. Les zébus paraissent mieux adaptés à des climats chauds et secs, les N'Damas à des climats chauds et humides.

Compte tenu des travaux déjà présentés et du fait qu'il est impossible de faire un exposé complet sur le sujet en dix minutes, il m'a semblé qu'en ce qui concernait plus particulièrement l'élevage dans les régions tropicales, il convenait de mettre l'accent sur deux problèmes d'importance majeure:

1. l'action des facteurs climatiques sur les *besoins en eau*;
2. l'action des facteurs climatiques sur la *répartition de l'eau dans l'organisme animal.*

En effet, dans les zones tropicales arides, la recherche de l'eau est un problème de vie ou de mort et on peut dire que tous les animaux domestiques vivant dans les zones arides ont soif en permanence, puisqu'ils ne sont souvent abreuvés que tous les deux ou trois jours.

L'action dépressive du facteur «abreuvement» est augmentée par les variations saisonnières de la qualité des fourrages; pendant six à huit mois de l'année les animaux n'ont à leur disposition que des pailles sèches de valeur fourragère médiocre, souvent carencées en oligo-élements (fer, cuivre, cobalt, ...).

Les recherches sur les besoins en eau des animaux ont été conduites aussi bien sur le terrain qu'en chambre psychrométrique. Les résultats des premières sont peut-être moins précis mais ils sont d'un intérêt indéniable pour les éleveurs, c'est pourquoi nous mettrons l'accent sur ceux qui ont été publiés au cours des dernières années et qui semblent caractéristiques, ne pouvant les citer tous.

Ainsi, Rollinson (1955) en Uganda, étudiant les réactions des zébus de race locale entretenus en élevage extensif sur des pâturages naturels a trouvé que ces animaux buvaient entre 7 et 19 heures, 9,04 kg d'eau alors que pendant le même temps des animaux témoins à l'étable n'en consommaient que 4,98 kg. Toujours en Uganda, Wilson (1961) a trouvé que les animaux buvaient pendant la saison sèche une quantité d'eau représentant 8,8 pour cent du poids vif et pendant la saison de pluies 5,1 pour cent.

Dans des observations conduites au Mali où le climat est de type tropical soudanien avec schématiquement une saison des pluies de quatre mois, une saison sèche de huit mois, nous avons comparé les besoins en eau de deux lots de bovins entretenus en élevage extensif sur un pâturage naturel et abreuvés une fois par jour.

Ces lots de bovins appartenaient l'un à l'espèce B. indicus, l'autre à l'espèce B. taurus; les deux races employées, race peulh pour les premiers, race N'Dama pour les seconds, vivent depuis le début des temps historiques en Afriques, elles y sont parfaitement acclimatées, c'est-à-dire que la fécondité est normale, les vaches donnent suffisamment de lait pour nourrir leur veau et leur croissance, compte tenu des ressources fourragères spontanées, peut être considérée comme normale.

Les taurins N'Dama ont de plus une caractéristique spécifique, ils sont trypanotolérants; cette dernière qualité les a fait choisir pour peupler depuis une vingtaine d'années les savanes du Congo-Brazzaville et de la République Centrafricaine où en 1945 il n'y avait aucun élevage bovin.

Bamako, où furent conduites les expériences, se trouve localisée à la limite sud de l'aire de dispersion des zébus et à la limite nord de celle des taurins.

Etudiant donc les besoins en eau, nous avons observé que pendant la saison des pluies lorsque les températures ambiantes étaient basses, 28° C et le degré hygrométrique élevé, 65 pour cent, à une élévation de la température correspond une augmentation de la consommation d'eau alors qu'un accroissement du degré hygrométrique a une action inverse.

Si les zébus et taurins réagissent de façon très voisine à l'action de la température, les taurins réagissent d'une façon plus nette aux variations du degré hygrométrique.

Pendant cette période, la consommation est minimale, 10,4 l pour les zébus, 7,42 l pour les N'Dama.

Au cours de la saison sèche, lorsque la température a une valeur moyenne, 30 à 32° C, et que le degré hygrométrique est faible, 13 à 15 pour cent, l'action des variations de température est très faible et identique dans les deux groupes, alors que

Tableau 1. Besoins en Eau des Taurins et des Zébus en Zone Tropicale (A.O.F.)

Mois	Températur moyenne à 15 heures	Degré hygrométrique moyen à 15 heures	Evaporation journalière moyenne	Teneur moyenne en eau des fourrages	Eau consommée en litres	
					Zébus	Taurins
Janvier	30,22	13,15	6,23	29,40	21,62	21,62
Février	32,28	15,87	8,96	21,60	22,62	25,12
Mars	32,94	13,75	9,48	9,56	23,74	22,74
Avril	35,47	27,71	8,15	8,18	27,33	23,46
Mai	38,71	28,71	8,11	10,09	28,85	23,28
Juin	33,71	42,16	3,78	78,61	23,16	18,94
Juillet	30,18	59,20	2,54	75,25	19,66	16,08
Août	28,42	65,25	1,51	74,07	11,33	7,55
Septembre	29,68	69,37	1,47	71,09	10,42	7,42
Octobre	32,05	41,30	2,66	62,83	12,19	13,00
Novembre	31,15	42,16	3,35	51,87	12,49	16,16
Décembre	28,25	27,37	6,85	41,86	16,49	19,74

l'action des variations du degré hygrométrique est très nette et plus élevée chez les zébus que chez les taurins.

Pendant cette période, la consommation est maximale, 28,85 l pour les zébus, 23,46 l pour les N'Dama.

Au cours de la période qui se situe à la fin de la saison sèche, début de la saison des pluies, lorsque la température est élevée, 33° C à 38° C, le degré hygrométrique élevé, 42 à 59 pour cent, les zébus et les taurins ont des comportements différents. Les variations de température ont une action très faible chez les taurins, négligeable chez les zébus.

La corrélation négative entre les besoins en eau et le degré hygrométrique est plus élevée chez les zébus que chez les taurins. Pendant cette periode les zébus consomment 22,6 l d'eau et les N'Dama, 25,12 l.

En résumé, les besoins en eau étant en fait une mesure de l'action des mécanismes thermorégulateurs, il semble que, chez les taurins comme chez les zébus, que ce soit surtout la valeur du degré hygrométrique qui intervienne dans leur régulation thermique, et lorsque la température atteint des valeurs voisines de la température corporelle, l'action du degré hygrométrique est bien plus forte sur les zébus que sur les taurins.

Compte tenu de la valeur des différents coefficients de corrélations partielles, les taurins supportent mieux les hauts degrés hygrométriques que les zébus.

Ces conclusions n'infirment pas les observations écologiques relatives à la répartition géographique des races N'Dama et zébus peulh, les zébus vivent dans les zones sahélienne et soudanienne, à climat tropical sec huit à neuf mois par an, les taurins dans la zone guinéenne et équatoriale humide huit mois sur douze.

Poussant plus loin nos investigations, nous avons trouvé ques les rythmes cardiaque et respiratoire, la température rectale, étaient tout au long de l'année plus

Tableau 2. Coefficient de Corrélation entre les Besoins d'Eau et la Température Extérieure

	1ère période	2ème période	3ème période
Zébus r_{BT}	$+0{,}569 \pm {}^{0{,}098}_{0{,}120}$	$+0{,}293 \pm {}^{0{,}108}_{0{,}117}$	$+0{,}724 \pm {}^{0{,}070}_{0{,}091}$
Taurins r_{BT}	$+0{,}657 \pm {}^{0{,}082}_{0{,}101}$	$+0{,}266 \pm {}^{0{,}110}_{0{,}120}$	$+0{,}543 \pm {}^{0{,}107}_{0{,}129}$
Différence	non significative	non significative	significative

élevés chez les N'Dama que chez les zébus. Zébus et N'Dama avaient des courbes de croissance et des productions comparables. Ainsi, nous semble-t-il, qu'il convient d'être très prudent dans l'interprétation des résultats expérimentaux lorsqu'il s'agit de choisir une race nouvelle pour le milieu considéré.

Envisageant le deuxième problème qui nous intéresse, à savoir l'action des facteurs climatiques sur la répartition de l'eau dans l'organisme animal, nous signalerons quelques expériences et observations qui intéresseront certainement les éleveurs des régions tropicales. Wilson et Philips (1960) ont trouvé que les zébus consommaient significativement moins d'eau par kilo de grain et par kilo de foin que les Hereford entretenus dans les mêmes conditions.

Dans leur travail, ils signalent que si les animaux ne reçoivent que la moitié de l'eau qu'ils buvaient lorsqu'ils pouvaient boire à volonté, la consommation de foin était réduite de 65 pour cent pour les Hereford et de 61 pour cent pour les zébus; si le rationnement portait sur le foin (70 pour cent) la consommation d'eau diminuait de 15 pour cent.

Tableau 3. Coefficient de Corrélation entre les Besoins en Eau et le Degré Hygrométrique

	1ère période	2ème période	3ème période
Zébus $r_{B.H.}$	$-0{,}635 \pm {}^{0{,}105}_{0{,}086}$	$-0{,}741 \pm {}^{0{,}062}_{0{,}051}$	$-0{,}830 \pm {}^{0{,}061}_{0{,}045}$
Taurins $r_{B.H.}$	$-0{,}737 \pm {}^{0{,}085}_{0{,}064}$	$-0{,}653 \pm {}^{0{,}078}_{0{,}064}$	$-0{,}549 \pm {}^{0{,}128}_{0{,}106}$
Différence	significative	significative	significative

Tableau 4. Coefficient de Corrélation entre les Besoins en Eau et l'Evaporation Journalière Moyenne

	1ère période	2ème période	3ème période
Zébus $r_{B.E.}$	$+0{,}533 \pm {0{,}105 \atop 0{,}125}$	$+0{,}623 \pm {0{,}070 \atop 0{,}081}$	$+0{,}673 \pm {0{,}080 \atop 0{,}104}$
Taurins $r_{B.E.}$	$+0{,}658 \pm {0{,}074 \atop 0{,}115}$	$+0{,}788 \pm {0{,}040 \atop 0{,}052}$	$+0{,}819 \pm {0{,}048 \atop 0{,}064}$
Différence	significative	significative	significative

Negi et Mullick, aux Indes, avaient noté que la quantité de matières sèches consommées par de zébus des race Kumauni était, par jour, de 892 g par 100 kg de poids vif, à 20° C et seulement de 744 g à 35° C.

Un effet secondaire du rationnement en eau est l'accroissement de la digestibilité du foin que nous avons observée comme French l'avait signalé.

Les observations faites à Dakar par M. Labouche montrent que la technique ulitisée pour mesurer l'eau interstitielle manquait de reproductibilité, ainsi, deux essais pratiqués sur le même animal à quelques jours d'intervalle ont donné les deux valeurs suivantes: 24,4 et 15,5 pour cent du poids vif.

Avec cette méthode, il a trouvé que chez les vaches zébus l'eau interstitielle représentait 16,8 pour cent du poids vif en moyenne, les chiffres trouvés variaient de 10,4 à 20,4 pour cent; l'écart entre les chiffres extrêmes étant encore plus grand chez les veaux, 9,8 à 27,1, moyenne 16,9.

Dans des essais de rationnement d'eau effectués en vue d'élucider l'étiologie d'une affection qui se caractérise par une deshydratation accompagnée de perte de la soif, M. Labouche (1963) limitant l'abreuvement de vaches nourries exclusivement avec du foin a trouvé que *l'urémie* passe de 11 à 25 cg et se stabilise à ce niveau. En supprimant complètement l'eau, l'urémie atteint très rapidement 67 cg et se stabilise à cette valeur (maximum individuel 107 cg) la courbe de croissance du taux de l'urée est de type exponentiel; l'état général est meilleur mais on note dunediminution de la consommation de tourteaux pendant les derniers jours.

La reprise de l'abreuvement s'accompagne d'une chute rapide de l'urémie.

En ce qui concerne l'excrétion urinaire, il nous semble à la lecture des recherches céjà effectuées que, si on a pu mettre en évidence des corrélations entre l'eau ronsommée et les quantités d'urine émises, nombre de détails du mécanisme de la ésorption de l'eau de filtration glomérulaire reste encore à élucider, les recherches conduites par M. Labouche et ses collaborateurs au Laboratoire de l'Elevage de Dakar dont les résultats sont en cours de dépouillement, fourniront certainement quelques éclaircissements.

Tableau 5. Coefficient de Corrélation Partielle entre les Besoins en Eau et la Température à Humidité Constante et le Coefficient de Corrélation Partielle entre les Besoins en Eau et l'Humidité à Température Constante

	1ère période	2ème période	3ème période
Zébus $r_{BT.H.}$	$+0{,}319 \pm \frac{0{,}137}{0{,}152}$	$-0{,}269 \pm \frac{0{,}118}{0{,}111}$	$+0{,}184 \pm \frac{0{,}156}{0{,}167}$
Taurins $r_{BT.H.}$	$-0{,}421 \pm \frac{0{,}124}{0{,}142}$	$-0{,}199 \pm \frac{0{,}121}{0{,}115}$	$-0{,}229 \pm \frac{0{,}165}{0{,}153}$
Différence	non significative	non significative	non significative
Zébus $r_{BH.T.}$	$-0{,}457 \pm \frac{0{,}119}{0{,}147}$	$-0{,}737 \pm \frac{0{,}072}{0{,}051}$	$-0{,}608 \pm \frac{0{,}118}{0{,}095}$
Taurins $r_{BH.T.}$	$-0{,}582 \pm \frac{0{,}116}{0{,}097}$	$-0{,}638 \pm \frac{0{,}079}{0{,}068}$	$-0{,}208 \pm \frac{0{,}166}{0{,}154}$
Différence	significative	significative	significative

En terminant, je voudrais indiquer que si j'ai insisté sur les observations faites sur le terrain, ce n'est pas pour minimiser les travaux de recherche fondamentale conduits avec des moyens et appareillages souvent considérables, mais plutôt pour montrer ce qui pouvait être tiré des découvertes de la recherche fondamentale par ceux qui sont en contact avec les éleveurs et leurs problèmes.

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DER EINFLUSS DES WETTERS AUF DEN TÄGLICHEN MILCHERTRAG BEIM RIND

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Abstract – An investigation was made of the effect of weather on the milk yield of cows. In a comparison of the milk yield of 24 cows over one complete lactation with 6 successive weather phases, as defined by Ungeheuer, it was found that milk yield tended to be elevated in the "settled" phases 2 and 6 and to be depressed in the "unsettled" phases 3 and 4. The two "settled" phases were known from work on man to have a stimulating effect on the sympathetic nervous system ("sympatico-tonic"), the two 'unsettled' phases on the vagus ("vagotonic"). The sensitivity to these weather phases varied from animal to animal and seemed to be associated with characters important in breeding. The degree of weather sensitivity might be an aid for predicting an animal's breeding value.

Zusammenfassung – Über die Dauer einer Laktation wird an 24 Fleckviehkühen, mit Hilfe der Wetterphasen nach Ungeheuer, die Abhängigkeit der täglichen Milchleistung vom Wettergeschehen nachgewiesen. Im Gegensatz zum biologisch ungünstigen Wetter (vagotone Reizlage) der Wetterphasen 3 und 4 geben die Tiere an Tagen mit biologisch günstigem Wetter (sympathikotone Reizlage) der Wetterphasen 2 und 6 in der Regel mehr Milch als am Tage zuvor. Ebenso liegt die Milchleistung an diesen Tagen über dem durch Berechnung des monatlichen Mittels markierten Trend der Laktationskurve. Die über die Milchleistung festgestellte Reaktion auf biotrope Reize ist für das Einzeltier charakteristisch und erscheint brauchbar, um über den Zuchtwert des entsprechenden Tieres eine Voraussage abgeben zu können.

Résumé – On a pu prouver que les types de temps selon Ungeheuer avaient une influence sur la production laitière de 24 vaches de la race tachetée rouge et blanche. Ces essais se sont étendu sur une lactation entière. Durant les jours où la situation est biologiquement favorable (sympathicotonique) soient les types 2 et 6, les vaches donnent en général plus de lait que la veille. Au contraire, durant les jours défavorables (vagotoniques) des types 3 et 4, elles en donnent moins. La production laitière est, dans le premier cas, supérieure à la valeur correspondante indiquée par le mouvement de la courbe de lactation calculée au moyen des moyennes mensuelles. La réaction aux stimulants biologiques constatée à la production laitière est caractéristique pour chaque individu et semble utilisable pour la prévision de la production en se basant sur la valeur individuelle de chacun d'eux.

EINLEITUNG

Obwohl die Bedeutung der Temperatur als physikalischer Teilfaktor des Klimas auf die Leistung des Rindes genau untersucht wurde, wissen wir doch nicht, ob das Wetter als Ganzes in seiner täglichen Veränderlichkeit auch innerhalb dieses biologisch günstigsten Temperaturbereichs die tierische Leistung beeinflußt.

Die Untersuchungen, über deren Ergebnisse ich hier berichte, sollen einmal zur Klärung dieser Frage beitragen und zum anderen darüber Aufschluss geben, ob es auch hier individuelle Unterschiede in der Reizbeantwortung gibt.

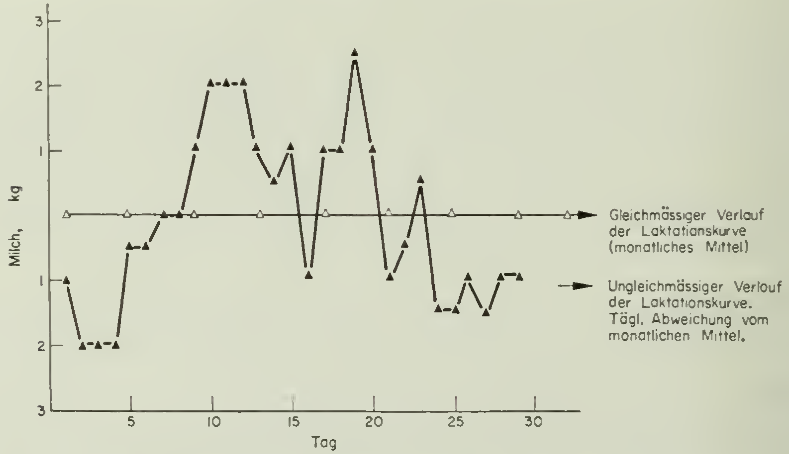


Abb. 1. Tägliche Abweichung (ungleichmäßiger Verlauf) von dem durch das monatliche Mittel festgelegten gleichmäßigen Laktationsverlauf beim Rind

Es wird dabei von der Hypothese ausgegangen, daß die Milchleistung im Rahmen einer Laktation bis auf die ersten Wochen nach Laktationsbeginn einen gleichmäßig abnehmenden Verlauf hat. Dieser wird durch eine Vielzahl von Faktoren beeinflußt, z. B. durch Fütterung oder Krankheit. So kommt es je nach Art der Einwirkung zu Abweichungen vom gleichmäßig abnehmenden Verlauf der Laktationskurve in Form von Leistungssteigerungen oder Leistungsminderungen (Abb. 1). Ähnlich verhält es sich mit dem Wetter. Dieses ist für jeden Ort spezifisch und in seinem jährlichen rhythmische Ablauf ebenfalls gleichmäßig. Durch äußere Einflüsse, wie etwa fremdbürtige Luftmassen, die von der Höhe her oder aus entfernten geographischen Bereichen einwirken, kommt es zu Abweichungen vom gleichmäßigen Ablauf. Je nach Art dieser sogenannten fremdbürtigen Luftmassen kommt es zu Steigerungen oder Dämpfungen des herrschenden meteorologischen Milieus (Ungeheuer, 1955). So werden in Wirklichkeit beide, Milchleistung und Wetter, meist nicht in ihrer gleichmäßigen sondern in ihrer ungleichmäßigen, von fremden Einflüssen geprägten Verlaufsform angetroffen.

Ungeheuer (1955) hat nun den tatsächlichen, durch fremdbürtige Luftmassen geformten Wetterablauf idealisiert und in 6 Phasen eingeteilt. Jede dieser Phasen kennzeichnet einen ganz bestimmten Zustand des herrschenden Wetters, das aus dem geordneten Zusammenspiel aller erfaßbaren meteorologischen Faktoren resultiert (Abb. 2). In diesem idealisierten Ablauf kommt dem Wetter der Wetterphase 2 ein sympathischer und damit leistungssteigernder Effekt zu, während die Wetterphasen 3 und 4 mehr vagoton wirkende, d. h. leistungsmindernde Wetterlagen bezeichnen.

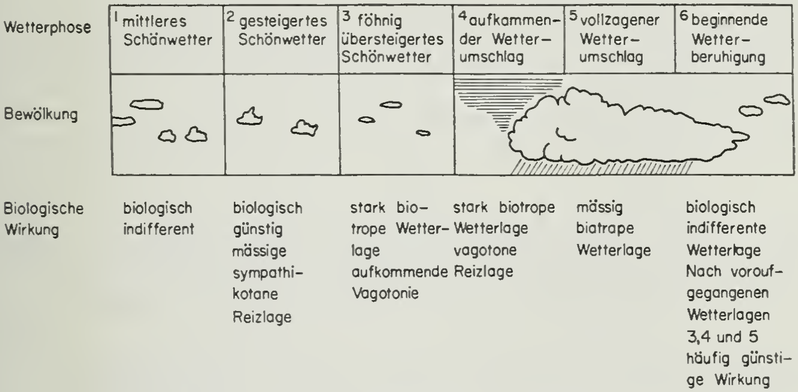


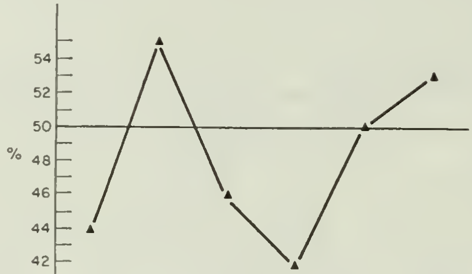
Abb. 2. Die Wetterphasen nach Ungeheuer und ihre Wirkung auf den Organismus

Wenn nun die Abweichungen vom gleichmäßigen Laktationsverlauf durch das Wetter mitbedingt sind, müssen die Zunahmen gegenüber dem Tage vorher vor allem auf die Tage der günstigen, sympathikotonen Wetterphase 2 fallen, wogegen auf Tage mit den vagotonen Wetterphasen 3 und 4 verhältnismäßig wenig Zunahmen gegenüber dem Tage zuvor kommen dürften.

Eigene Untersuchungen

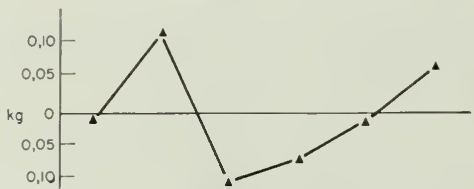
Bei 24 Fleckviehkühen, die bezüglich der Fütterung und Haltung unter gleichen Bedingungen standen, wurde die tägliche Milchmenge im Verlauf einer Laktation gemessen (Meßgenauigkeit 0,1 kg). Aus Abb. 3, geht hervor, daß die Tiere an 714 Beobachtungstagen mit der Wetterphase 2 an 390 Tagen, also in 55% der Fälle mehr Milch als am Tage zuvor gaben. Demgegenüber wurde an 1217 Tagen mit der Wetterphase 4 nur an 516 Tagen, das ist in 42,3% der Fälle eine höhere Milchleistung als am Tage zuvor verzeichnet. Der Gesamtablauf der Leistungsänderungen entspricht der biotropen Wirkung des Wetters, d. h. einer überdurchschnittlichen Steigerung gegenüber dem Tage zuvor bei Wetterphase 2, wogegen die Hauptzahl der Leistungsabfälle auf Tage mit Wetterphase 3 und 4 fallen.

Bei der quantitativen Auswertung wurden gleichlaufende Zusammenhänge gefunden. Der gleichmäßige Laktationsverlauf wird hier durch den mit Hilfe des monatlichen Mittels festgelegten Trend der Laktationskurve dargestellt (vergl. Abb. 2). An 523 Beobachtungstagen (Abb. 4) mit der Wetterphase 2 liegt die Milch-



1	2	3	4	5	6	Wetterphasen
44	55	46	42	50	53	Prozentualer anteil
34–67	36–72	30–62	23–61	37–65	40–86	Individuelle streuung
756	714	717	1217	847	1168	Beobachtungstage
331	390	331	516	422	615	Tage mit Zunahme gegenüber dem Tage zuvor

Abb. 3. Prozentualer Anteil der Tage mit Leistungszunahme gegenüber dem Tag zuvor in ihrer Verteilung auf die einzelnen Wetterphasen (100 = Gesamtanzahl der Zunahmen an Tagen mit der entsprechenden Wetterphase)



1	2	3	4	5	6	Wetterphasen
−0,01	+0,12	−0,10	−0,07	−0,01	+0,07	Durchschnittliche Abweichung in kg pro Tier und Tag
+0,3 −0,4	+0,3 −0,1	+0,3 −0,3	+0,1 −0,2	+0,2 −0,3	+0,3 −0,1	Individuelle Streuung
493	523	483	782	508	872	Beobachtungstage

Abb. 4. Durchschnittliche Abweichung der täglichen Milchleistung (= ungleichmäßiger Laktationsverlauf) vom monatlichen Mittel (= gleichmäßiger Laktationsverlauf) an Tagen der einzelnen Wetterphasen pro Tier und Tag in kg Milch

leistung im Durchschnitt pro Tag und Tier 0,12 kg über dem Wert des regelmäßigen Laktationsverlaufs. An 782 Beobachtungstagen mit der Wetterphase 4 jedoch liegt die Milchleistung im Durchschnitt pro Tier und Tag um 0,07 kg unter dem Wert des regelmäßigen Laktationsverlaufes. Die Gesamtabweichungen, geordnet nach Wetterphasen, entsprechen auch hier dem Biotropismus der Wetterphasen. Die durchschnittlichen, täglichen Abweichungen vom gleichmäßigen Laktationsverlauf (Trend) gemessen in kg sind jedoch so gering, daß sie, auf bestimmte Einzeltiere und Tage bezogen, kaum ins Gewicht fallen. Das liegt daran, daß die absolute Milchmengenleistung von einer Reihe Faktoren, z. B. Fütterung, Krankheit, Melker, ganz erheblich und weit stärker als durch die biotropische Wirkung des Wetters beeinflußt wird. Man rechnet mit einer Heritabilität der Milchleistung von etwa 0,3. So bleibt also, und das scheint vom physiologischen Geschehen her richtig, die Richtung der Abweichung vom gleichmäßigen Verlauf entscheidend. Dies lässt sich jedoch nur sichern, wenn die Beobachtung über einen genügend langen Zeitraum durchgeführt wird.

Es kann den vorausgegangenen Erhebungen nach kaum bezweifelt werden, daß das täglich wechselnde Wetter auf das Rind einen Einfluss ausübt. Dieser beeinträchtigt zweifellos auch die Behaglichkeit des Rindes, was bei den Wetterlagen der Wetterphasen 3 und 4 in einer Abnahme der Milchleistung zum Ausdruck kommt.

Diese biotropen Reize sind nicht an einen bestimmten Temperaturbereich gebunden und kommen in- und außerhalb des eingangs umrissenen biologisch günstigen Temperaturbereichs zur Geltung.

Die individuellen Unterschiede in der Reizbeantwortung sind erheblich. Es kann im allgemeinen zwischen Tieren unterschieden werden, die sehr starken wetterbedingten Leistungsänderungen unterworfen sind und solchen, bei denen sich Wetteränderungen kaum bemerkbar machen. Darüber, welche Art der Reizbeantwortung der einzelnen Tiere noch physiologisch und welche schon krankhaft ist, läßt sich vorläufig kaum eine verbindliche Aussage machen. Auf Grund der Nachkommenprüfung der untersuchten 24 Kühe jedoch scheinen die überempfindlich reagierenden Tiere, d.h. jene mit größeren, häufig auftretenden Abweichungen bei den entsprechenden Wetterphasen züchterisch weniger wertvoll zu sein (Abb. 5). Die untersuchten 24 Tiere erbrachten insgesamt 103 Kälber. Davon entwickelten sich 30 schlecht, kamen tot zur Welt, starben vor der Schlachtreife, hatten schlechte Gewichtszunahmen oder mußten später abgegeben werden, weil sie nicht trächtig wurden. Ihr Anteil beträgt 29%. Von den 22 Kälbern der 6 überempfindlich reagierenden Tiere entsprechen nur 11 den gestellten züchterischen Erwartungen. Ihr Anteil beträgt also 50%. Von den 16 Kälbern der 3 Tiere jedoch, die gering auf die biotropen Reize reagierten und sich gegen die äußeren Einflüsse gut abschirmen oder diese ausgleichen konnten, schieden nur 2, d.i. 12,5% aus.

Der Wettereinfluß auf die täglichen Milchertragsschwankungen steht in seiner Stärke sicher hinter der Wirkung von Fütterung, extremen Temperaturänderungen und dergleichen zurück und kann deshalb, nicht zuletzt auch auf Grund methodischer Schwierigkeiten, nur in seiner Tendenz aufgezeigt werden. Es ist auch denkbar, daß bei einer weiteren Aufteilung der Wetterphasen, die durch Brezowsky (1960) vorgenommen wurde, eine deutlichere Aussage getroffen werden kann. (Tabel, 1963).

	Zahl der Muttertiere	Zahl der geborenen Kälber	Davon unterlagen mangelnder Entwicklung oder Krankheit mit Todesfolge	%
	24	103	30	29
Davon entfallen auf überempfindlich auf Wetterreize reagierende Tiere	6	22	11	50
Verhalten auf Wetterreize reagierende Tiere	3	16	2	12,5

Abb. 5. Anteil der Kälber mit mangelnder Entwicklung oder Krankheit mit Todesfolge von überempfindlich und Verhalten auf Wetterreize reagierenden Muttertieren

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DIRECT CALORIMETRY IN ANIMAL THERMOREGULATION RESEARCH—A THEORETICAL APPROACH

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Abstract – A method is presented whereby the unique capabilities of the Benzinger thermoelectric system of direct calorimetry can be exploited to increase understanding of thermoregulation. The homeothermic animal's system for temperature regulation is modeled into a closed loop circuit in which the hypothalamus functions as error-detector, controller and measuring means. The "process" is rate of radiation heat loss, and the final control elements are the blood vessels in the surface vascular bed. Temperature of the hypothalamus is taken at the tympanum. Differential equations are used to describe the behavior of the closed loop.

Zusammenfassung – Es wird eine Methode beschrieben, mit deren Hilfe die grossen Möglichkeiten des thermoelektrischen Systems der Direktkaloriemetrie nach Benzinger ausgenützt werden können, um zu einem besseren Verständnis der Temperaturregelung des Körpers zu gelangen. Im Modell eines geschlossenen Kreislaufs funktioniert der Hypothalamus als Fehler-Detektor sowie als Kontrollorgan und Messgerät. Die Grösse der Wärmeabstrahlung entspricht dem 'process' und die oberflächlichen Blutgefässe stellen die letzten Kontrollelemente dar. Das Verhalten dieses geschlossenen Kreislaufs wird anhand von Differentialgleichungen beschrieben.

Résumé – On décrit ici une méthode par laquelle les immenses possibilités du système thermoélectrique de la calorimétrie directe selon Benzinger peuvent être utilisées en vue d'une meilleure compréhension de la thermorégulation des corps. L'hypothalamus fonctionne comme détecteur d'erreurs dans le modèle d'un circuit fermé ainsi que comme organisme de contrôle et d'appareil de mesure. L'importance de la chaleur rayonnée correspond au processus et les canaux sanguins périphériques représentent les derniers éléments de contrôle. On décrit le comportement de ce circuit fermé au moyen d'équations différentielles.

INTRODUCTION

The purpose of this paper is to outline a theoretical approach in order to further understanding of thermoregulation in the farm animal through exploitation of the thermoelectric calorimeter system of Benzinger and Kitzinger (1949) in conjunction with automatic control theory. The thermoregulation to be considered is limited to the physical regulation which occurs at environmental temperatures above thermoneutrality; such limitation is indicated because the typical farm animal, such as the cow, is less adapted to cope with high temperatures (Brody, 1945) and therefore the housing problem is more acute under such conditions.

The Benzinger system consists in a temperature-difference (gradient) thermopile, having about $^1/_4$ to 2 junctions per square inch (about 0.03 to 0.31 cm^2), mounted as the continuous inner lining of a chamber sized appropriately to the animal to be studied. The thermopile voltage output is a linear function of the rate of heat transferred from the subject. A water jacket is provided around the chamber to permit precise temperature control of the gradient thermopile. For measurement of evaporative heat loss a system of "plate meters" is used which, among other functions, precisely conditions the temperature and humidity of the entering ventilation air.

Benzinger and Kitzinger (1950) also proposed a 4 π radiometer thermopile, superimposed on the gradient thermopile and capable of partitioning the radiation heat loss from the other forms of sensible heat dissipation. The principle was adopted by Stewart (1957) and improved by Mason (1962).

The Benzinger system has been adopted with modifications by several investigators (Lawton, Prouty and Hardy, 1954; Pullar, 1956; Stewart, 1957; Mason, 1962; Jordan and Dale, 1963; Walton and Dale, 1963). It has many advantages over the older methods of direct calorimetry, such as rapid response and continuous recording of the heat loss; further, the heat loss is partitioned into convection-conduction, radiation and evaporation.

The system can easily be combined with indirect calorimetry through gas analysis of the ventilation air stream as used by Lawton, Prouty and Hardy (1954).

It is, therefore, postulated that a complete Benzinger calorimetric system is available as outlined above, is of proper size, and has an overall accuracy within 5 per cent. The thermoregulatory behavior of cattle and similar large animals has not been studied by use of such a system; such studies are needed, and it is hoped that this paper might stimulate work of this kind.

REGULATORY RESPONSES ABOVE THERMONEUTRALITY

There is some degree of indecision in locating an exact site in the homeotherm where temperature is precisely regulated. Hardy and Hammel (1963) assume that the "average" body temperature is regulated. Benzinger (1959) assumes that the temperature of the blood perfusing the hypothalamic region of the brain is precisely regulated because a small change in its temperature caused regulatory action in man.

The nature of the regulatory mechanism is also somewhat open to question. Benzinger, Kitzinger and Pratt (1963) believe that central regulation by the hypothalamus is amply proved through human experiments. Others, such as Fusco, Hardy and Hammel (1961) have found much evidence in the dog and in man that the regulation is composed of summative action of a system having both central and peripheral components. Probably the homeothermic regulation can display both characteristics, depending on the kind of loads imposed and the conditions surrounding the experiment.

For the purposes intended in this paper, it is necessary to first assume the simplest case before proceeding to the more complex. The simplest case, it appears, would be that where central regulation is assumed, where the tympanic temperature is the regulated internal entity, and where vasomotor response to heat is the major output of the control system.

The above assumptions ignore, for the present, two items: (a) the possible reflex vasomotor activity caused by skin temperature change, and (b) the control parameter embodied in change of evaporation rate through change in respiration rate. Formation of perspiration at high ambient temperature is rare in cattle, while evaporative heat loss from the lungs and nasal passages in cattle undergoes a small change even when respiration rate changes radically (Brody, 1945; Kibler, Brody and Worstell, 1949). Thus, neglect of the second item is probably more valid than neglect of the first; it is dangerous to ignore the possibility of reflex vasomotor response mediated directly by changes in skin temperature, or mediated by peripheral control elements. The risk is accepted only in order to construct a model whose assumed attributes can be most readily confirmed or denied by simple calorimetric experiments.

A BIOLOGICAL ANALOGY TO AN AUTOMATIC CONTROL SYSTEM

Part of the homeostatic activities can be regarded as controlling and controlled mechanisms wherein the energy input to the system is some function of the output itself. This appears to be true on most levels, ranging from cellular to organismic (Brody, 1945). Homeothermy is a special case in the complex of control mechanisms known as homeostasis. The principle of feedback control is widely distributed in nature and its study should promote insight and provide models worthy of man's imitation.

Investigation of thermoregulation as an analog to the engineering of automatic process control has received attention in the recent past, usually with special reference to dog and man. Particular attention is called to the work of Crosbie, Hardy and Fessenden (1963), and of Hardy and Hammel (1963). Mason (1962) extended the concept to the rabbit; using the Benzinger system at the University of Missouri, he found that thermoregulative action at high temperatures was in good correspondence with his theoretical closed-loop analog.

These investigations, and others, have helped to establish the possibility that homeothermy can be properly viewed as an analog to the electromechanical automatic control systems of science and industry. It is beginning to appear also that the character, or modes of action, of these systems and their mathematical descriptions have definite application to the homeotherm. This is important because development of mathematical treatments of the various thermoregulatory events should lead to more comprehensive experiments and a more reliable interpretation of the events (Hertzman, 1963).

In Fig. 1 a basic closed-loop system is illustrated which has a fixed set-point and a variable load. The system is basic because it contains the minimum number of elements necessary to be operable.

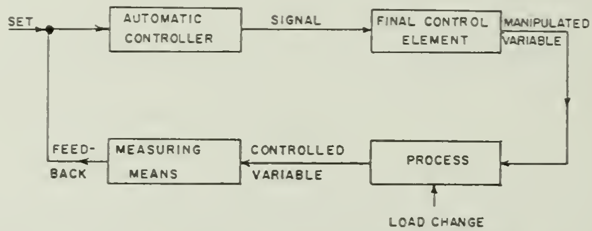

Fig. 1. Figure 1 is a conventional, mechanical, automatic control system containing the essential elements for operation

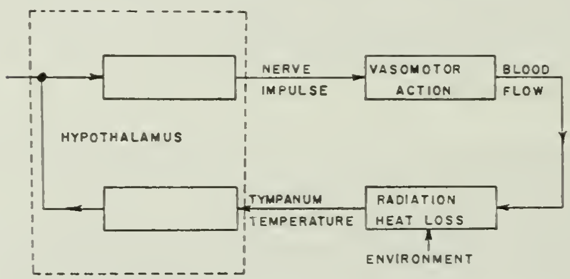

Fig. 2. A biological analog related to Fig. 1. In the analog it is assumed that the reference input, automatic controller, measuring means, and feedback pathway are all contained in the appropriate tissues of the hypothalamus. The analogy is simplified by the assumption that peripheral control mechanisms are lacking in the animal. This assumption is made solely for purposes of simplification

Figure 2 shows the presumed biological analog of Fig. 1. The five essential parts of Fig. 1 have been converted to their counterparts in the animal by use of the assumptions set forth in the preceding section of the paper. The conversion is simple, straightforward, and grossly oversimplified.

The "process" is that which functions to produce a controlled variable. In the biological analog the process is chosen to be one which operates at the intersection of the animal and the climate surrounding it. Radiation heat exchange is chosen as the process because it is instantly responsive to a load change which affects surface temperature and because it is rapidly integrated into a voltage output by the radiometer of a Benzinger system. Thus, advantage is taken of the property that transitory changes in surface temperature can be both brought about and measured in the Benzinger system. When based on measurement of the 4 π net radiation exchange, the system offers a unique method for study of surface temperature behavior as a process involved in regulation of internal temperature.

The characteristics of the analog are summarized as follows:

a) Controller, Reference input, Measuring means = Hypothalamus,
b) Controller output signal = Nerve impulses,
c) Final control elements = Vasomotor action,
d) Manipulated variable = Peripheral blood volume rate of flow,
e) Process = Rate of radiation heat loss,
f) Load change = change in physical environment (temperature, humidity, etc.),
g) Controlled variable = Tympanic temperature.

CALORIMETRIC STUDY OF THE ANALOG

To determine the characteristic dynamic behavior of a process or control component, an input is artificially applied and the output response that follows is observed. Patterns of typical input signals are: (a) the step function, (b) the sinusoidal function.

Dynamic Response to the Step Function

The step function response can be viewed as a record of the method by which additions and losses of energy in a process take place. A step input can be applied at any part of a closed-loop control system. It is a small, rapid change in set-point, final control elements, or load, etc. Sometimes one part of the system is uncoupled in order to apply a step function to another part. The step function response of a closed-loop is a way of determining the basic characteristics of the system. These are: (a) the dead time, (b) the time constant, which results from resistances and capacitances in series, (c) the presence or absence of linearity in the system. It is proposed that the step function be a load change.

The dynamic response of a first-order system can be described by a linear first-order differential equation (Eckman, 1958). The following factors must now be defined:

θ = value of the animal radiation heat loss,
θ_F = final value of radiation heat loss,
e = natural logarithm base,
t = time,
T = time constant of the animal system, the product of thermal resistance times capacitance.

If the system is first-order the step function response is

$$T\frac{d\theta}{dt}+\theta = \theta_F \tag{1}$$

The particular solution of (1) is

$$\frac{\theta}{\theta_F} = 1-e^{-t/T} \tag{2}$$

Equation (2) indicates that: (a) the output–input ratio increases exponentially, (b) the ratio approaches 1 asymptotically (c) when $t=T$, 63 per cent of the response is completed.

Use of equation (2) would proceed as follows. The subject would be placed in the chamber where the environmental conditions are held near the upper limit of thermoneutrality. After attaining a steady-state value in θ the environmental temperature would be raised sharply upward 5° or 10° C. The radiometric apparatus would follow and record θ until attainment of θ_F. During this time it would be necessary to record the tympanic temperature. If appreciable change in this temperature follows the step function, followed by a rather rapid change in surface temperature, it may be argued that the overall animal system is responding by vasodilatation. Examination of the radiometric record should then yield numerical values for the dead time and the time constant of the overall system.

If prefered, the step function response may be studied as surface temperature because this is related to the radiation heat loss. For a body whose surface area is small (12 to 1 or less) compared to the interior surface area of the calorimeter chamber, the following factors are defined:

Q_r = radiation heat loss,
R = effective radiating surface area of the animal body,
E = emissivity of the body surface,
S = Stefan–Boltzmann constant,
T_s = integrated effective surface temperature,
T_w = calorimeter wall temperature.

By the Stefan–Boltzmann equation:

$$Q_r = RES(T_s^4-T_w^4),\ T_s > T_w \tag{3}$$

By the assumption that the animal body area is small relative to the chamber wall area, the animal body is radiating within a black body and the emissivity of the interior walls becomes unity.

Reasonable values for R can be determined in the calorimeter chamber by measurement of Q_r, by measuring T_s and T_w directly and by use of $E \cong 0.98$. Equation (3) is then solved for R and the measured values substituted in order to determine R.

Having determined the appropriate factors, equation (3) should next be solved for T_s:

$$T_s = \left[\frac{EST_w^4 + \dfrac{Q_r}{R}}{ES}\right]^{\frac{1}{4}} \tag{4}$$

The step function response could now be measured in terms of initial and final values of T_s. The difficulty with use of equation (4) lies in making the change in T_w rapidly enough so that T_w can be viewed as a constant at the new value. If T_w is constant while T_s responds to the step function, then Q_r becomes the variable on the right side of equation (4). Perhaps the most straightforward approach would be to deal with θ rather than T_s.

The total animal regulatory system mechanisms are likely to be of higher order than the first. If so, the step function response is complicated by damping phenomena. For example, a second-order response may be oscillatory where the damping ratio is less than unity. The rate of radiation heat loss, however, seems unlikely to exhibit oscillatory response; therefore, a damping ratio of unity can be assumed. This type of transient is described by:

$$\frac{\theta}{\theta_F} = 1 - e^{-t/T}\left[1 + \frac{t}{T}\right] \tag{5}$$

whose characteristic curve can be studied by plotting dimensionless ratios, θ/θ_F versus t/T.

Response to a Sinusoidal Input

The step function response is a transient. The question of linearity of the animal control system may not be quite settled by the step function response. Sinusoidal analysis can help determine the order of the response mechanisms; the response of a linear system to a sinusoidal input is sinusoidal and of the same frequency as the input. With Benzinger calorimetry available this aspect should be interesting to study.

Let

A = cycle amplitude in temperature units,
w = circular frequency of the cycle,

then the general response equation for a first-order system is:

$$T\frac{d\theta}{dt} + \theta = A \sin wt \tag{6}$$

The steady-state solution is of value rather than the transient. The frequency response, or steady-state solution, is:

$$\left[\frac{\theta}{A}\right]_{ss} = \frac{1}{\sqrt{1+(wT)^2}} \sin(wt - \theta) \tag{7}$$

where

$\theta = \tan^{-1} wT$, or phase lag,

ss = steady state

The expression $1/\sqrt{1+(wT)^2}$ is the amplitude ratio, showing that the output signal is attenuated by increasing the circular frequency of the input. The time constant, T, has previously been determined.

The phase lag can be converted into time units by:

$$\text{Time lag} = \frac{\tan^{-1} wT}{w} \tag{8}$$

Determination of the amplitude ratio and the phase, or time, lag could be accomplished by equipping the Benzinger system with "program" controllers. These would operate in a coupled fashion to change the air and wall temperatures simultaneously according to the selected sinusoidal pattern.

Properties of the Control Action

The typical control system can have three possible modes of action or a combination of these: (a) proportional; (b) integral or reset; (c) derivative or rate. The familiar "on–off" controller may be regarded as a proportional controller with zero per cent proportional band. Generally, proportional action is the basis for the controller mechanism; where the other modes of action are employed, they are interlocked with, and superimposed upon, the proportional mode.

The characteristic that determines control output in the proportional mode is size and direction of deviation or error. The greater the deviation the greater the corrective action until the controller is "saturated," i.e. incapable of further control output.

To consider the control modes and possible methods of study in the farm animal, it would probably be convenient to use integrated surface temperature as the output signal, since the radiometric portion of the calorimeter chamber can follow this as shown in equation (4). To suggest the procedure for determining the proportional constant, the following are defined:

T_0 = surface temperature at thermoneutral conditions (zero error condition),
T_s = surface temperature,
T_1 = initial tympanic temperature,
T_2 = tympanic temperature after change,
e = error signal = $T_1 - T_2$,
b = proportional constant, dimensionless.

The output signal is directly proportional to the error signal:

$$T_s = \frac{1}{b}\,(T_1 - T_2) + T_0 \tag{9}$$

and

$$b = \frac{T_1 - T_2}{T_s - T_0} \tag{10}$$

It should be noted that equation (10) is somewhat similar to that used by Hardy and Hammel (1963) in study of thermoregulation in the dog.

Two means are available to find b. One way would be to manipulate the load by a fast upward step function in environmental temperature. The other way would consist in manipulation of the error signal e, as was done in the human by Benzinger (1959). Both methods should probably be tried.

Note the importance of the initial assumption that sole controlling action lies in the hypothalamus and that tympanic temperature is the measure of the error signal. Possible peripheral control action, for example, would leave the error signal unchanged after a load change. Also, the tympanic temperature may not reflect hypothalamic temperature accurately. These sources of possible difficulty must not be ignored when interpretation of results is necessary. Surgical entry into the hypothalamic area itself might ultimately be called for.

A proportional controller allows the controlled variable to leave the set point after appreciable load change has occurred. This is known as "offset". The control mode which returns the variable to the set point is called integral or reset. The integral mode of action is related to the error signal as follows:

$$T_s = f \int e \; \mathrm{d}t + T_0 \tag{11}$$

where f = integral constant or reset rate, in units of reciprocal of time. Equation (11) can be rewritten as:

$$T_s - T_0 = f \int (T_1 - T_2) \; \mathrm{d}t \tag{12}$$

Equation (12) shows that when an error occurs, the total change of the output signal is equal to the area under the curve of error versus time.

The argument for the presence of integral or reset control in animal thermoregulation is weak. The regulation mechanisms do not move the body temperature back into the neutral range during continued high thermal loads. A mechanical control system would repeat the proportional action until return to set point is obtained.

However, the mechanism of "acclimatization" through hormone alteration of metabolic rate might be viewed as a reset form of action beyond hypothalamic regulation. Thus, the short-term regulation may not display reset action, while the long-term climatic adjustments may well do so.

Equation (12) could be used to study the possible presence of an integral constant. An error signal might be induced through heating the tympanum or by introduction of heated material into the rumen.

The derivative or rate mode of control operates only when the error signal is changing. The output signal is proportional to the rate of change of the error signal.

The rate mode is an anticipating action which seeks to restore the variable to the set point at some period of time in advance of that which the proportional mode alone would achieve. This explains why, in physical systems, the rate constant is often expressed in units of time.

A relation between rate action and error signal is:

$$T_s = r\frac{\mathrm{d}e}{\mathrm{d}t} + T_0 \tag{13}$$

or

$$T_s - T_0 = r\frac{\mathrm{d}(T_1 - T_2)}{\mathrm{d}t} \tag{14}$$

where r = rate constant, time units.

The rate mode is valuable in controlling processes which have considerable lag. Such a lag can be visualized in the animal control system path between vascular valve action and the subsequent change in temperature of the blood returning to the control center (Stewart, 1963). An initial "overshoot" response is needed; such response has been pointed out in the human (Benzinger, 1963) and in the dog (Hardy and Hammel, 1963).

The rate constant could be determined through observation of the time variation in the error signal after a step function in the environmental temperature.

In conclusion, the preceding proposals are preliminary and elementary. For example, much further development of the analog could be made, culminating in equations for the transfer functions.

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ANIMAL THERMONEUTRALITY AS A THERMODYNAMIC RATE PROCESS

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Abstract – Thermodynamically, the living system is regarded as being open at constant pressure and temperature; temperature gradients are not essential to biological function so the system cannot be regarded as a heat engine. The first two laws apply. As a chemical rate process, the biosystem tends toward stationary state. This state is the one which has the lowest possible rate of entropy production, and is completely stable. By analogy, thermoneutrality is a state of minimum energy dissipation or entropy production. The thermodynamics of irreversible processes is used to develop the analogy and to predict possible experimentation

Zusammenfassung – In thermodynamischer Hinsicht stellt der lebende Organismus ein offenes System dar, in dem Druck und Temperatur konstant sind. Das Vorhandensein von Temperaturgefällen ist nicht unbedingt notwendig für das Funktionieren des biologischen Systems; dieses kann somit nicht als eine „Wärmemaschine" betrachtet werden. Die ersten zwei thermodynamischen Gesetze finden Anwendung. Da das Biosystem einen chemischen „rate process" darstellt, tendiert es gegen einen stationären Zustand hin, der eine minimale Entropieerzeugung hat und der vollkommen stabil ist. Analog hierzu ist die Thermoneutralität ein Zustand minimaler Energieabgabe oder Entropieerzeugung. Die Thermodynamik irreversibler Vorgänge wird dazu verwendet, die Analogie herzustellen und um mögliche experimentelle Befunde vorherzusagen.

Résumé – Au point de vue thermodynamique, l'organisme vivant représente un système ouvert dans lequel pression et température sont constantes. La présence d'un gradient thermique n'est pas absolument indispensable au fonctionnement du système biologique. On ne peut donc le considérer comme une machine thermique. Les deux premières lois de la thermodynamique peuvant lui être appliquées. Comme le système biologique représente un processus chimique nécessitant un certain gradient, il tend vers un équilibre stationnaire qui a une entropie minimum et est absolument stable. Par analogie, le neutralisme thermique est un état de dégagement énergétique minimum. La thermodynamique de processus irréversibles est utilisée à provoquer cette analogie et utilisable pour prévoir les possibilités de résultats expérimentaux.

THERMAL neutrality, or thermal zero, is the environmental temperature zone at which heat loss from the homeotherm is equal to the minimum heat production (Brody, 1945): it occurs in a zone of temperature in which the physiological temperature regulation is largely by physical means. Ideally, the environmental temperature is adjusted to keep the body temperature normal without employment of regulation mechanisms.

It is proposed in this brief discussion that the thermal behavior of the animal at thermoneutrality be examined with the aid of thermodynamics of irreversible processes, or rate processes. Classical thermodynamics treats generally of equilibrium states and the transitions from one equilibrium state to another. It provides theory only for reversible processes, with much interest in the heat engine. Nonequilibrium phenomena, such as heat flow, are irreversible, or rate processes, and such processes play a significant role in the thermal behavior of living systems. Fortunately, such phenomena can be treated in the steady-state condition (Prigogine, 1961).

To apply thermodynamics of rate processes to the thermoneutral homeotherm it is necessary to define the conditions and assumptions.

The total system is assumed to be open, or exchanging matter and energy with the environment; therefore, in contrast to the isolated system, the entropy of the open system can decrease with time, particularly during growth (Prigogine, 1961). The system is assumed to operate at constant volume and constant pressure, such that there is little difference between energy and enthalpy in Gibbs' free energy function. External work and storage of heat through change in body temperature are excluded; growth is likewise excluded.

Temperature gradients occur in the system, but they are not essential to the basic biological functioning; therefore, the second law of thermodynamics is applied to a uniform temperature device in which it is impossible to convert heat into work. The analogy to the heat engine is not valid for the living system.

In a system at constant temperature the degradation of free energy is a measure of the inefficiency of the system (Wilkie, 1960). The creation of entropy is the criterion of such degradation. The warm-blooded animal degrades free energy at an exceptional rate, thus permitting maintenance of a high body temperature; the concept in this paper is that at thermoneutrality the free energy degradation is at a minimum as measured by the rate of entropy production.

Under appropriate constraint of conditions in the environment Prigogine (1961) stated that the stationary or steady state may to a good approximation be considered in the living system as a state of *minimum* (not zero) production of entropy per unit time. He points out that this concept harmonizes well with the known stability of living organisms against external perturbations. The analogy to the thermoneutral state is therefore created.

To be considered valid in nonequilibrium thermodynamics, a transport process description is limited to linear phenomenological laws such as Fourier's law. The applicability of Fourier's law of heat flow to the homeotherm was recently clarified by Kleiber (1963) when he objected to the use of Newton's law of cooling. Newton's law applies to the rate of temperature change of a warm body in a cool environment; the homeotherm maintains a *constant* inner temperature, however. The simplest equation for heat flow from core to surface is thus better described by

Fourier's law:

$$\frac{dQ}{dt} = \frac{A}{r_1}(T_b - T_s) \tag{1}$$

in which Q = heat, t = time, A = surface area, r_1 = thermal resistance, T_b = core temperature and T_s = surface temperature. Thus the irreversible heat flow can be expressed as proportional to a temperature gradient. There is no inconsistency between the heat flow temperature gradient and the requirement that the living system operate isothermally. The latter requirement refers to the complex chain of chemical and physical processes which give rise to heat that must be transported in the living organism across the gradient of temperature and dissipated at the surface–environment interface.

Considering only the entropy produced by the irreversible heat flow, the change in entropy between core and surface is

$$\Delta_s = \frac{Q}{T_s} - \frac{Q}{T_b} \tag{2}$$

or

$$\Delta_s = Q\left[\frac{T_b - T_s}{T_b T_s}\right] \tag{3}$$

in which S = entropy.

Passing to the limit, the rate at which entropy is produced during the heat flow is

$$\frac{dS}{dt} = \frac{dQ}{dt}\left[\frac{T_b - T_s}{T_b T_s}\right] \tag{4}$$

Referring back to equation (1), the heat flowing from core to surface must also flow from surface to environment, on a gradient proportional to $(T_s - T_e)$, where T_e = environmental temperature.

$$\frac{dQ}{dt} = \frac{A}{r_2}(T_s - T_e) \tag{5}$$

Substituting (5) into (4), one obtains

$$\frac{ds}{dt} = \frac{A}{r_2}\frac{(T_s - T_e)(T_b - T_s)}{T_b T_s} \tag{6}$$

noting that r_2 = thermal resistance at surface.

Equation (6) represents a relation between entropy production and the temperatures of the core, the surface and the environment. It suggests that simple temperature measurements will permit determination of the overall rate of entropy creation. However, difficulties associated with determination of surface area and heat transfer coefficients render the experimental procedures somewhat complex.

If the experimenter can measure heat production accurately, either by direct or indirect methods, use of Fourier's law will yield an approximation of the resistance coefficient. Surface area can be estimated from the weight. A more elegant means is offered by the thermoelectric system of Benzinger (1949) with addition of 4 π radiometer (Stewart, 1957) in which surface temperature and surface area can be directly measured as well as the heat flow, dQ/dt.

The thermoneutral state is therefore theorized to be the state of minimum entropy production. This theory is logical if it can be assumed that heat production increases with rising temperature above thermoneutrality. In animals such as cattle this may not occur because of decreased feed intake and other reasons. Such being the case, the system is completely altered and the argument in this paper would not apply. The present argument is valid where Fig. 11.11 of Brody (1945) is assumed to be valid.

It is tempting to compare the thermoneutral state in physiology to the principle of least action in mechanics. In mechanics, for a conservative system, the time integral of the Lagrangian function has a stationary value for the actual path compared with all other paths having the same end-points and performed in the same time. In most cases the stationary value is a minimum. The system is in stable equilibrium only under those conditions for which its potential energy is at a minimum.

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FEED INTAKE IN THERMOREGULATION AND PERFORMANCE UNDER HIGH TEMPERATURES

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Abstract – An animal's heat tolerance is modified by a number of factors and it appears that nutritional level can have as much or more effect in thermoregulation as other factors. Nutrition enters into the seasonal acclimatization in that cattle wintered under high nutrition suffer more than low plain animals in the spring and early summer months. It is evident that many of the physiological changes that were formerly attributed to high environmental temperatures are direct effects of feed intake and feed quality. Feed intake appears to be regulated by the animal's ability to dissipate the heat of food metabolism.

Zusammenfassung – Die Hitzetoleranz eines Tieres wird durch zahlreiche Faktoren bestimmt, unter welchen die Grösse des Futterkonsums offenbar eine wesentliche Rolle spielt. Die Fütterung beeinflusst die saisonale Akklimatisation des Rindes; Tiere, die im Winter auf einem hohen Fütterungsniveau standen, leiden im Frühling und Frühsommer mehr unter der Hitze als Tiere, die auf einem niederen Fütterungsniveau gehalten worden waren. Viele der physiologischen Veränderungen, die bisher als direkte Einwirkungen der hohen Umgebungstemperatur betrachtet wurden, sind tatsächlich auf Veränderungen der Futteraufnahme und der Futterqualität zurückzuführen. Die Grösse der Futteraufnahme scheint bestimmt zu werden durch die Fähigkeit des Tieres, die durch den Futterstoffwechsel erzeugte Wärme abzugehen.

Résumé – La tolérance à la chaleur d'une bête est déterminée par de nombreux facteurs parmi lesquels la consommation de fourrage joue vraisemblablement un rôle important. L'affouragement influence l'acclimatement saisonnier du bétail. Des bêtes qui ont été richement nourries en hiver souffrent plus du chaud au printemps et au début de l'été que d'autre moins bien affouragées. Il n'y a aucun doute que bien des modifications physiologiques étaient considérées jusqu'ici comme la conséquence directe de températures ambiantes élevées sont en fait à mettre au compte de changements dans la qualité et la quantité de fourrage consommé. La quantité de fourrage consommé semble déterminée par la capacité de l'animal d'éliminer la chaleur produite par son métabolisme.

Our current knowledge of heat adaptation in domestic animals may be summarized by stating that the animal which performs most satisfactorily under hot conditions does so because of: (a) differences in the capability of promoting heat loss; (b) differences in the efficiency of energy utilization; or (c) differences in the ability to tolerate compensatory responses.

Thus far efforts have been directed principally toward comparative differences in heat loss. The results indicate breed and individual differences but when the data on ability to dissipate heat are assembled they do not explain adequately the observed differences in responses to hot and/or humid conditions. The belief is growing that the efficiency of energy utilization is also an important factor in performance under hot conditions. However, this must not be carried to an extreme. Low heat production will favor heat adaptability or tolerance, but it must be remembered that the physiological conditions responsible for or accompanying a low basal rate may so reduce the productive performance that any expected economic advantage may be significantly offset.

Under field conditions, with the onset of environmental temperature conditions above the "critical level" for most domestic animals, there is usually a concomitant rise in the fiber in the forages available. Thus the animal is placed in double jeopardy by both the direct and indirect effects of the climate. It is the intent of this report to summarize some of the findings on feed intake in evaluating heat adaptation and the importance of feed quality under hot humid conditions.

Temperature regulating mechanisms may be divided into two main areas: (a) physical, those not involving changes in heat production and consisting of changes in circulation, respiration, surface evaporation, and hair thickness and length; (b) chemical, those which involve changes in heat production by shivering, decreased thyroid activity and decreased feed intake.

It is a commonly observed fact that the level of feeding directly affects the level of rumen volatile fatty acid (VFA) production. Weldy (1962) found that the total rumen VFA concentrations were highly correlated with feed intake (0.49) and with rectal temperature (−0.78). The acetic acid fraction was largely responsible for the lower values. The reasons for these changes could not be ascertained, but one or more of the following may be involved: (a) high body temperatures are detrimental to certain rumen micro-organisms; (b) stressed animals may have a higher rate of passage through the intestinal tract; (c) increased water intake may cause a dilution of the rumen contents; and (d) decreased feed intake may simply lower rumen VFA production. Blood glucose as well as blood ketones are highly correlated with feed intake (Weldy, 1962). If the heat production is lowered by these and other methods, the animal under thermal stress would have less heat to dissipate and theoretically show less response.

In the field of chemical regulating mechanisms, Bonsma *et al.* (1940) state that the quantity of heat generated in the body of cattle is directly proportional to the amount of total digestable nutrients consumed. Furthermore, the amount of feed consumed is determined by the animal's ability to dissipate the heat of food metabolism (Ragsdale *et al.*, 1948). Gaalaas (1945), however, reported that feeding had no appreciable effect on body temperatures in his field studies. Blaxter and Wainman (1960) state studies of heat emission showed that losses per unit of surface area by convection, conduction and radiation were unaffected by the level of nutrition.

Various researchers have found that high environmental temperatures bring about decreased feed intake, under field and laboratory conditions, which tends to complicate interpretation of the measurements of heat stress. With lowered feed intakes it is often difficult to separate true acclimatization from "physiological wisdom", the term used by Ragsdale *et al.*, (1948) to describe the animal's need to reduce feed intake to a level where it can dissipate the heat of food metabolism and the heat of milk synthesis. Brobeck (1948) working with rats, found that food intake definitely appears to be controlled as if it were a mechanism of temperature regulation. In his work an attempt was made to relate the amount of food eaten to the animal's ability to dissipate the heat of food metabolism. If this is true it could be the key to a never ending feed back mechanism. Consequently, if the body temperature of an animal rises as a result of a high environmental temperature it consumes less feed in an attempt to reduce the metabolic heat production; then, a decline in the feed consumption may be a leading cause in lower milk production. While Yeates (1956) found well fed cattle less heat tolerant than poorly fed cattle, there are two important factors to consider in this relationship. First, a high level of nutrition may reduce heat tolerance not only by raising the resting metabolic rate, but also by causing interference with heat loss through the deposition of fat under the skin. On this matter it is of interest that Zebu type cattle seem to lay down fat preferentially in the interior of the body, while European type cattle do so under the skin (Ledger, 1959). Secondly, it has been shown by Yeates (1956) that an important factor in the feeding/heat tolerance relationship is the current rate of feeding. In other words, how much the animal has eaten shortly before the heat tolerance test is of importance in evaluating the data obtained; and a period of starvation before the heat tolerance test will help in obtaining reproducible results. However, since animals must eat to live and produce during heat tolerance tests, the animal which utilizes its food more efficiently, must be considered most heat tolerant.

The data on efficiency in relation to temperature are rather inconclusive. King (1963) reports chickens have the best rate of gain at 55° or 65° F, but efficiency of feed conversion is best at 95° (the highest temperature studied). In cattle, Johnson and co-workers (1957, 1959) at Missouri, in raising cattle and rabbits for one year at constant high (80° or 83° F) or moderate (48° or 50° F) environmental temperatures have demonstrated a depressing effect of the high temperatures on growth. They found the European-evolved cattle (Shorthorn, Holstein, Brown Swiss and Jersey) were markedly smaller while the Zebu types (Brahman and Santa Gertrudis) were less affected. McDowell *et al.* (1960), working with yearling Milking Shorthorn heifers kept at a constant 90° F for 36 weeks and pairmates at 30°–50° F, found no difference between the groups in either the rate of gain or feed efficiency. Both groups were fed a high energy, low fiber, finely ground ration in a pelleted form. In the same type of study, Bond *et al.* (1961), noted a significant decrease in the rate of gain and the efficiency of gain in Angus and Milking Shorthorn heifers under the same conditions. The animals kept at 90° F gained 0.33 lb/day and required 18.1 lb. feed/lb. gain, while the pairmates at 30°–50° F gained 0.60 lb/day and required only 9.4 lb. feed/lb. gained.

The Missouri workers (1957, 1959), state that feed intake is depressed in the European cattle at 75° to 85° F, and in the Zebu at 90° to 95° F. In this regard the results of Swett *et al.* (1961) may lend a possible explanation. They report that increasing the proportion of Sindhi inheritance in Jersey–Sindhi and Holstein–Sindhi crosses had the effect of reducing the size of the digestive organs independently of differences in body weight. These results indicate that the digestive

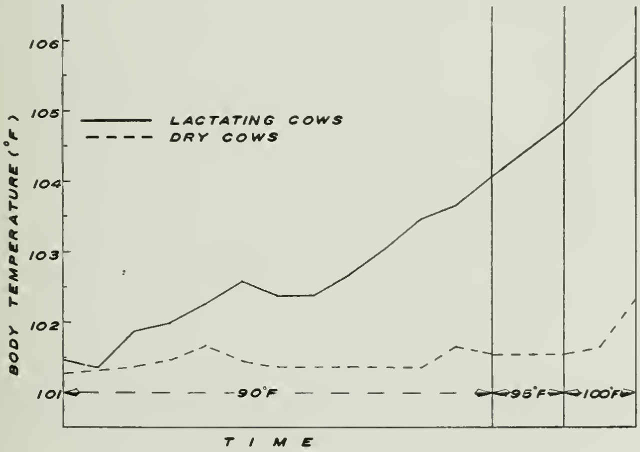

Fig. 1. Average body temperature of lactating and dry cows fed 100 per cent of requirements for 36 hr at 90° F, 4 hr at 95° F, and 4 hr at 100° F

organs of the Sindhis may limit the capacity for feed, thus avoiding peaks in feed intake and thereby result in a more constant metabolic heat production. If this is the case, the smaller digestive organs might be one of the characteristics responsible for the greater heat tolerance exhibited by Zebu types.

McDowell (1949), using mature lactating and non-lactating Holstein cows, studied the effect of feed intake on degree of response to changes in environmental temperature by making the following comparisons: (a) dry cows versus lactating cows when each group was fed according to requirements; (b) dry versus lactating when both groups were fed the amount of T.D.N. required by the lactating pair-mates; and (c) dry cows versus cows in the sixth month of lactation with both groups fed at the same level.

In the first comparison both groups were fed at 100 per cent of their requirements of a ration consisting of 90 per cent concentrate and 10 per cent long alfalfa hay. All cows were put on this ration 10 days before the trials. The T.D.N. intake of the lactating cows was 2 or 3 times greater than that of the dry cows. There was no appreciable difference between the groups at 65° F, but there was a markedly different reaction during the exposures to periods of 90°, 95° and 100° F (Fig. 1). The change in response may be due entirely to the difference in feed intake and the consequent different metabolic levels of the cows or to the combined effects of level of feed intake and the stimulus of lactation upon the basal metabolic rate. In the second trial, the dry and lactating cows were paired by weight and fed according to the total requirements of the milking pairmates, which meant some of

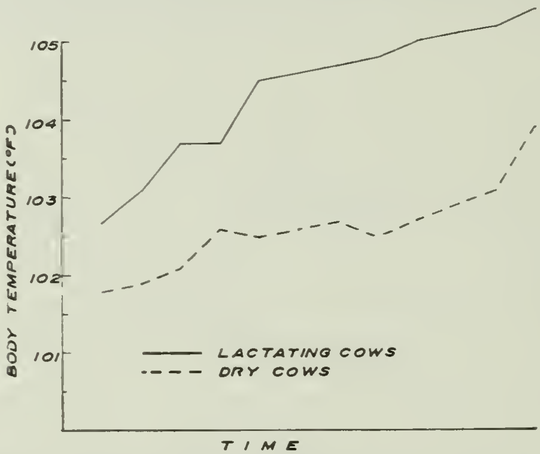

FIG. 2. Average body temperatures of lactating and dry cows, fed 100 per cent of the lactating cows requirements, for 36 hr at 90° F

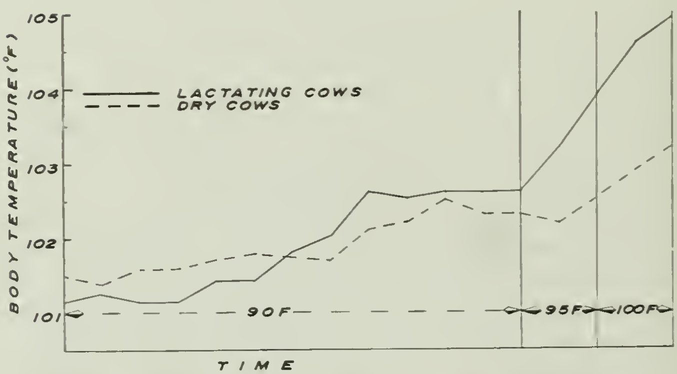

FIG. 3. Average body temperatures of 6th month lactating cows and dry cows, fed 100 per cent of the lactating cows requirements, for 36 hr at 90° F, 4 hr at 95° F, and 4 hr at 100° F

the dry cows were consuming from 200 to 300 per cent of their requirements. In this test the dry cows reacted more nearly like the lactating cows (Fig. 2). The dry cows showed an average increase in body temperature of 2.2° F during the 36-hr period compared to 0.3° F in the previous trial. However, there was still a definite difference in the degree of reaction of the dry and lactating groups, even though both groups consumed nearly the same amount of T.D.N. It is reasonable to assume that some factor other than feed intake is involved; possibly the lactating cows were drawing on body reserves in addition to the nutrients they consumed.

In a third trial dry and 6 month post-partum lactating cows fed at the same levels were compared. Virtually no difference was shown between the body temperatures until the groups were exposed to temperatures of 95° and 100° F. The feed intake of the lactating cows was undoubtly more closely related to the actual nutrient requirements for the total metabolic functions and show that feed intake is related to the response to thermal stress.

Wayman *et al.* (1962), using fistulated lactating cows, compared cows fed *ad libitum* with cows that were force fed any refusals. They conclude that the major decrease in milk production at high temperatures is due to reduced feed intake; however, high temperatures *per se* also cause a decrease in production. Part of this effect may be due to a decreased rate of passage through the rumen. They also noted that high temperatures caused a significant decrease in the efficiency of energy utilization for milk production.

Another area that appears to hold interest is the composition and form of the feed as high fiber rations are refused in greater amounts than are low fiber rations. Leighton and Rupel (1956) in field trials at the Texas station report that dairy cows on a high fiber diet produced less milk, had higher rectal temperatures and higher respiration rates than animals on a low fiber ration. They state that milk production was more sensitive to differences in the diet and to changes in air temperature than the other responses measured. In another trial (1960) these authors studied the effects of adequate versus high levels of protein in rations for dairy cattle. They found no significant differences, but the high protein diet was favored in all of the responses measured. Breidenstein *et al.* (1960) in a laboratory study at the Louisiana station compared rations containing 22 or 32 per cent crude fiber under cool (35 to 50° F) and summer (75 to 95° F) conditions. They found that the lower fiber rations were of benefit in maintaining milk production during hot conditions. In a further step, they broke down the treatment variance and found that 60 per cent of the variance in FCM production was associated with temperature, 34 per cent with fiber content and 6 per cent with the interaction of the two. Gross (1963), in an analysis of the climate of the 15 southernmost states in the United States, reports that while climate has a direct effect on milk production, "It appears that the indirect effects through a probable decline in the quality and/or quantity of forage may have a greater influence". He bases this belief on data obtained from the Louisiana station where they find that on the average, forages are available for grazing 352 days per year, but are sufficient in quality and quantity to support good milk production for only 133 days, with only 17 adequate days of grazing from 1 June to 1 November.

It appears from this evidence that the "methods or systems" of feeding is one of the major factors which may be used to prevent or lessen the summer slumps in milk production. The use of the proper types of forages, harvesting at the optimum low fiber-high T.D.N. levels and recognization of the fact that under certain climatic conditions forages tend to grow rapidly resulting in high fiber-low T.D.N. feeds must be taken into consideration for a well balanced feeding program.

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CARDIOVASCULAR RESPONSES OF THE OX *(BOS TAURUS)* TO HYPERTHERMIA

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Abstract – Recent work on the responses of the cardiovascular system of the ox to heat is described. An increase of arterial blood pressure and heart rate and vasodilatation in the extremities occur when: (a) the anterior hypothalamus is heated, (b) an area of the skin is exposed to infrared irradiation or (c) the entire body of the animal is exposed to heat. The cardiac output increases during exposure to heat.

Zusammenfassung – Es werden neuere Arbeiten beschrieben über Reaktionen des Kreislaufs beim Rind auf atmosphärische Hitze. Unter den nachfolgenden Bedingungen findet ein Anstieg des arteriellen Blutdrucks und der Herzfrequenz sowie Vasodilatation in den Extremitäten statt: (a) Wenn der vordere Hypothalamus erwärmt wird, (b) wenn ein Teil der Haut mit Infrarot bestrahlt wird, oder (c) wenn der gesamte Körper des Tieres erwärmt wird. Während der Wärmeexposition steigt die Menge des vom Herzen ausgeworfenen Blutes an.

Résumé – On décrit ici des expériences récentes de réactions du système cardiovasculaire du boeuf à la chaleur. Une augmentation de la tension artérielle, des battements du coeur, et de la vasodilation dans les extrémités, se produit quand: (a) on chauffe l'hypothalamus antérieur, (b) la surface de la peau est exposée à l'action de radiations infra-rouges, ou (c) on expose le corps entier de l'animal à la chaleur. La puissance cardiaque augmente pendant l'exposition à la chaleur.

During *hyperthermia* the respiratory rate and the minute volume of the ox increase and the tidal volume decreases until the deep-body temperature is approximately 40.5° C. This type of breathing is known as *thermal polypnoea.* It can occur, when the skin is heated, in the absence of any increase in the temperature of the thermoregulatory centres in the hypothalamus (Findlay and Ingram, 1961; Ingram and Whittow, 1962b). Localized heating of the anterior hypothalamus also causes thermal polypnoea but the magnitude of the increase in respiratory rate and minute volume produced by heating the hypothalamus is dependent on the environmental temperature (Ingram and Whittow, 1962a). When the deep-body temperature exceeds approximately 40.5° C thermal polypnoea appears to break down. The respiratory rate decreases and the tidal volume increases until the animal is removed from the climatic room when its deep-body temperature has reached 42° C. This change in the pattern of breathing during hyperthermia seems to be characteristic of panting animals. It has been observed in the sheep (Alexander and Williams, 1962), the rabbit (Marsh, 1954), the dog (Hemingway, 1938) and the chicken (Frankel, Hollands and Weiss, 1962). Evidence has been presented that the temperature sensitivity of the hypothalamus is involved in the response (Ingram and Whittow, 1962a). The purpose of this paper is to summarize the changes which occur in the cardiovascular system of the ox during thermal polypnoea and during the deeper breathing which supersedes polypnoea at high body temperatures.

When an ox is standing in an environment of approximately 15° C its extremities are cool and its respiratory rate low. If the anterior hypothalamus is heated under these conditions respiratory rate increases and tidal volume decreases. These changes are associated with large increases in the skin temperatures of the extremities (Ingram and Whittow, 1962a; 1963) which are presumably brought about by increases of blood flow to the extremities (Whittow, 1962). The arterial blood pressure and heart rate also increase (Whittow and Ingram, 1963). It is uncertain whether the increase in blood flow through the extremities follows passively the increase in blood pressure or whether it involves an active change in the calibre of the arterioles in the extremities. The cause of the increase in blood pressure is not known; it may be the result of an increase in cardiac output or of an increase in resistance to blood flow in vascular beds other than the skin. The increases in blood pressure and heart rate during heating of the hypothalamus are dependent upon the environmental temperature; the higher the environmental temperature, the greater the increase in both blood pressure and heart rate. Measurements of cardiac output have not yet been made during local heating of the hypothalamus. However, it seems possible that the increased pressor response to heating the hypothalamus at the higher environmental temperatures, might be brought about by an increased cardiac output because the response of the heart rate is greater at the higher environmental temperatures.

Although localized heating of the hypothalamus causes an increase in the skin temperature of the extremities, in blood pressure and in heart rate, such increases can also occur during localized infrared irradiation of the skin and in the absence of an increase in the temperature of the hypothalamus (Ingram and Whittow, 1962b; 1963).

When the ox is exposed to a severe heat stress both the deep-body temperature and the temperature of the periphery increase. Arterial blood pressure, heart rate and respiratory rate also increase (Whittow and Ingram, 1963). The greater part of the increase in arterial blood pressure has usually occurred by the time that the body temperature has reached approximately 40.5° C, i.e. at a time when the respiratory rate has reached a peak and the respiratory tidal volume is minimal. However, the heart rate continues to increase and the rate of increase is greater at body temperatures above approximately 40.5° C than below (Bianca, 1958). At deep-body temperatures of approximately 41.5° C, there is evidence that both the percentage of red cells in the blood and the specific gravity (of the plasma) increase (Bianca, 1957). The viscosity of the blood must therefore have increased.

Preliminary experiments performed by the author suggest that these changes are associated with an increased *cardiac output*. When the blood pressure in the heart or large arteries in the thorax of the ox is measured by means of long plastic catheter systems, a striking *modulation of* the *blood pressure wave* form is apparent at high body temperatures (Pichaicharnarong, 1960; Ingram and Whittow,

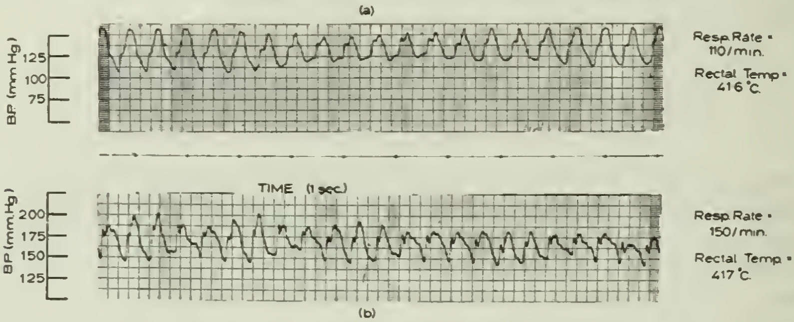

Fig. 1. Variations in pulse pressure and distortion of the blood pressure wave form in a hyperthermic ox. (a) and (b) represent separate exposures to an environment of 40° C dry bulb and 39° C wet bulb (Nisbet and Whittow, unpublished data)

unpublished data). A similar phenomenon has been observed by Nisbet and Whittow (unpublished data) who measured arterial blood pressure from an exteriorized carotid artery, using a measuring system with a high frequency response (Fig. 1). The cause of the observed changes in pulse pressure is not clear but on available evidence they are related to the respiratory rhythm.

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THE HEAT TOLERANCE OF SHEEP AND CATTLE IN RELATION TO FLEECE OR COAT CHARACTER

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Abstract – Cutaneous evaporation of sweat is the main avenue of heat dissipation in cattle. A short coat favours evaporation and hence facilitates hot-climate adaptation in this species. Sheep rely for their cooling more on respiratory tract evaporation, so their fleece is a less serious encumbrance; indeed, it is of overall benefit in shadeless country, as a protection against direct solar radiation. The ability of temperate zone cattle to shed their coat in spring, and the characteristic of equatorial breeds to maintain a short coat all the year round are genetic traits of high evolutionary significance. Selective breeding for appropriate coat characters can assist the tropical adaptation of introduced stock.

Zusammenfassung – Beim Rind ist die Verdunstung von Schweiss die wichtigste Art der Wärmeabgabe. Ein kurzes Haarkleid begünstigt die Verdunstung und erleichtert hiermit die Wärmeanpassung. Das Schaf dagegen stützt sich bei der feuchten Wärmeabgabe mehr auf die Atmungsverdunstung, sodass die Gegenwart eines Vlieses weniger stört. In einer Gegend ohne Schatten bildet das Vlies sogar einen wichtigen Schutz gegen Sonnenstrahlung. Die Eigenart der Rinder gemässigter Zonen, ihr Haarkleid im Frühling abzustossen, sowie die Eigenart der Rinder tropischer Zonen, das ganze Jahr hindurch ein kurzes Haarkleid zu bewahren, sind genetische Merkmale, denen eine hohe evolutionäre Bedeutung zukommt. Selektive Züchtung auf günstige Haarkleidmerkmale ist geeignet, die Anpassung eingeführter Tiere zu fördern.

Résumé – Chez les bovidés, l'évaporation de la sueur est le mode le plus important d'éliminer la chaleur. Un pelage court facilite cette évaporation et, par conséquent, l'adaptation au chaud. Le mouton utilise par contre davantage l'évaporation de l'eau dans ses organes respiratoires, si bien que la présence de laine est moins génante. Dans une région sans ombrages, une toison présente même une protection efficace contre les rayons du soleil. La particularité qu'ont les bovidés des zones tempérées de muer au printemps (c'est à dire de perdre leur toison laineuse), comme celle des bovidés des régions tropicales de garder toute l'année un pelage court, sont des caractéristiques génétiques auxquelles il faut attribuer une haute importance évolutive. Une sélection des meilleures caractéristiques du pelage est susceptible de faciliter l'adaptation de bêtes importées.

COAT AND SWEATING

The sheep derives only a minor part of its total cooling aid from sweating, whereas in cattle sweating occupies a major role (Knapp and Robinson, 1954). Further, within the different breeds, types and strains of cattle there are grades of sweating competence (e.g. Klemm and Robinson, 1955). Clearly, within such a series of animals (sheep and cattle), the relationship of coat type to sweating ability will be very important in determining the overall benefit of cutaneous evaporation.

It would seem best for an animal with good sweating ability to have a coat type which allows free movement of air over the skin, and hence the most efficient evaporation. This should be all the more important in hot-wet climates; not necessarily so important in the extremely hot-dry climates where evaporation is likely to be good despite an insulating layer of hair.

In an animal with poor sweating ability, on the other hand, there may be advantages in its having a protectice fleece or hair covering which will at least help to combat the heat increments of direct solar radiation. This will be so, however, only in so far as either the hot air is dry enough to permit efficient cutaneous evaporation despite the insulation, or the animal is equipped with a satisfactory alternative channel of heat dissipation such as the respiratory tract cooling of sheep.

In illustration of this point, sheep in a hot-room tolerate heat better when shorn than when in wool (Dutt and Hamm, 1957; Foote *et al.*, 1957), presumably because they are receiving some benefit from enhanced cutaneous evaporation; but sheep in direct hot sunshine show less stress with a fleece covering than without wool (Macfarlane *et al.*, 1958; Parer, 1963), no doubt because the slight benefit of enhanced evaporation with shearing is more than offset by an increased gain of heat from direct radiation. Parer has shown that the relationship between wool length and conduction of heat through the fleece is hyperbolic, a fleece less than 1 cm in length offering virtually no protection, with protection increasing rapidly beyond that length and reaching a maximum at about 4 cm.

Recognizing, then, that the explanation of heat tolerance involves understanding of the complex associations between (a) respiratory and cutaneous evaporation; (b) climate (including temperature, humidity, air movement and radiation); and (c) insulation, let us look in greater detail at those characteristics of the fleece or coat which appear to be important in thermal adaptation. Attention will be given mainly to cattle, since the climate physiology of sheep has recently been reviewed by Hutchinson and Wodzicka-Tomaszewska (1961).

COAT AND TEMPERATURE

Bonsma (1949) has been the pioneer worker in relating coat character to productivity in cattle in a tropical and sub-tropical environment. He demonstrated the superior growth, reproduction and thrift of smooth, as compared with wooly-coated individuals, and showed that coat type is of major importance in heat tolerance and a heritable character for which selection may be made soon after birth. It was also South African work, some by Bonsma but also by Riemerschmid and Elder (1945) which showed the differential absorption of infrared and ultra-violet radiation by different combinations of coat colour and hide pigmentation.

Recent progress, both in the climate laboratory (Yeates, 1955; Bianca, 1959) and in the field (Dowling, 1956; Turner and Schleger, 1960) has amplified and confirmed Bonsma's findings, but coat colour as such is not now accorded very high significance as a heat tolerance attribute. Despite the clearcut differences in the ability of different coloured coats to reflect incident radiation, greater emphasis is placed on sweating ability, glossiness and shortness of coat. This opinion seems justified by (a) the more recent findings that cattle do sweat quite appreciably (Klemm and Robinson, 1955; Ferguson and Dowling, 1955; McDowell *et al.*, 1961); (b) the fact that sweating makes such a substantial contribution to body cooling; and (c) Priestley's (1957) finding (which, though for sheep, probably also applies to some degree in cattle) that absorbed radiant energy is largely re-dissipated before reaching the skin surface. Certainly, at any rate, the minor differences (2 per cent) in reflectance between the light and dark shades of an intermediate colour like red should be quite unimportant in regard to heat tolerance. It should not, therefore, deter the breeders of Hereford cattle who, as in Australia, prefer a dark red coat in their cattle to the lighter, more yellow shade which is popular in America—especially since Schleger (1962) has shown the rich red colouration in the Australian Hereford to be associated with thrift and rate of gain.

From all the experimental studies, including those where clipping has been employed (e.g. Turner, 1962), the salient fact emerges that a dense mat of hair is prejudicial to the heat tolerance of cattle in hot, and particularly hot-wet environments. Among temperate zone cattle, shedding of the hair in spring is a natural adaptation to meet this difficulty, hence shedding will now be considered in more detail.

COAT SHEDDING

The seasonal pattern of changes in the coat character of cattle, and particularly the sudden and dramatic shedding of the hair in spring, has been shown by Yeates (1955) to be photoperiodically regulated. Good nutrition is also a requisite (Yeates, 1958), while it is common knowledge that diseases of a debilitating type such as tuberculosis impede the shedding process.

Despite the important part which light undoubtedly plays, it does not, however, account fully for all the observed coat phenomena. Thus general observation suggests that the winter coats of beef breeds like the Angus and Shorthorn and Galloways to take an extreme in long, shaggy coat probably never grow to such thickness and length in countries like Australia, South Africa and Argentina as they do in the Scottish homeland of those breeds. Moreover, even within Australia the winter coats of Angus and Shorthorns seem invariably to be thicker and possibly even slower to shed in the geographical regions which are colder, even though the places of comparison might be on the same latitude and, hence, photoperiodically similar.

These observations suggest a subsidiary influence of temperature. This is in fact supported by recent experiments of Berman and Volcani (1961) who even go so far as to postulate thyroid involvement as the likely mechanism, pointing out that L-thyroxine has direct peripheral effects on hair growth and colouration in cattle, and that thyroid secretion rate is known to be affected by ambient temperature.

Hayman and Nay (1961) believe that a second, minor, shedding of hair occurs in cattle in the autumn. Inherent in this view, which is inferred mainly from histological observations, is the belief that the long hairs of the winter coat are not the young summer ones grown old, but a new generation of special winter hairs; and hence that the majority, if not all, of the follicles grow two hairs in a year. This idea, that the winter hairs, starting anew, can grow so long, so quickly, seems hard to reconcile with visual appraisal of the coat *in situ* on the animals. Until further evidence is fortcoming, therefore, the view that, in cattle, full physiological shedding is an autumn as well as a spring occurrence should be accepted with some reservation.

BREED DIFFERENCES

The question of breed differences in shedding is perhaps best considered ecologically. Since shedding is largely controlled by light, it would be expected, by analogy with photoperiodically controlled seasonality of reproduction in sheep, that the breeds originating in the higher latitudes, where seasonal light differences are large, would exhibit the strongest seasonality in coat character; and that those originating in the tropics, where light is less changeable, would display the least. This appears to be so. The beef breeds of Scotland illustrate in their range from summer shortness to winter length of hair the extreme in changeability of coat type, so appropriate to their environment; while certain equatorial breeds, such as the Ankole cattle of Uganda maintain, obviously to their advantage in heat tolerance, the same short length of coat throughout the year. Other breed types illustrate an intermediate situation. The Africander, for example, like many other cattle of Zebu origin, displays a minor degree of seasonality, having a slightly thicker, longer coat in winter than in summer, and by shedding lightly, but definitely, in spring. All this is appropriate to the latitudes on the outer fringes of the tropics inhabited by these cattle; and it is no doubt a factor in the evolution of them as breeds. Indeed, so potent a factor does this adjustment seem to have been in evolution, that coat type in cattle, as well as their reactivity to imposed new light environments, could well be an aid in any classification of breeds in terms of their latitude of origin, where this is otherwise unknown.

In illustration of this latter suggestion, current observations* of Ankole cattle originally from Uganda, but now maintained at the Whipsnade Zoological Gar-

* Made by the author, through kind permission of the Zoological Society of London

dens in Bedfordshire, England, are showing that these animals display virtually no change in depth or thickness of coat throughout the year. They have preserved what is apparently their ancestral short, smooth hair character even in wintertime in a year of record low temperature, when snow has covered the countryside. Clearly, they lack in their inheritance the physiological mechanisms by which temperate zone cattle respond to seasonal changes, whether of light or temperature. Conversely, if temperate zone breeds are transferred to an equatorial environment, the indications from photoperiodic experiments are that their natural coat cycle is eliminated (Yeates, 1957).

DESCRIPTION OF COAT TYPE

While terms such as "short, sleek" or "long, woolly" are expressive and useful in referring to cattle coats, it is desirable for some purposes to use a greater degree of objectivity. This has sometimes been attempted by quoting the weight of clean, dry hair per unit area of skin surface following clipping from a measured patch on a stated position of the body. This, however, can be misleading as it takes little account of shedding, which proceeds at different rates and different times on the various body regions; also because it ignores such characteristics as glossiness and flatness of coat, and straightness and thickness of the hairs. Photography can be useful in overcoming some of these difficulties, while it also provides a permanent record. It is unsuitable for statistical treatment, however, and to meet this sort of need the "coat-score" approach has been adopted by Turner and Schleger (1960).

Their scoring system, though subjective, includes the feel as well as the appearance of the coat and has a numerical range from 1 to 7, these two end-points corresponding respectively to "extremely short" and "very woolly." Depth of coat is the primary criterion of classification, with "handle" (a subjective assessment of diameter of hairs) a modifying factor. Using this scale Turner and Schleger found coat character to be closely related to skin temperature and growth rate, (the smooth, sleek-coated animals having the lower skin temperatures and the faster weight gains).

Schleger and Turner (1960) selected depth of coat and hair diameter as criteria for coat description on the basis of an objective assessment which they made of the contribution of all the characters involved in overall coat type and growth rate. Of lesser importance, they found, were percentage of medullated hairs and the maximum length of fine hairs; hair curvature and follicle angle contributed little. These workers emphasise the greater value of coat score than any other assessment on the grounds that it refers to the whole coat *in situ:* it takes account of features of coat structure which are lost in hair samples. Their finding that medullation has no unique significance is of interest in view of the importance which other workers have attached to it.

HERITABILITY OF COAT CHARACTER

The task of fixing the short-coated character in cattle of European breeds, thus forming strains which are adaptable to heat, should not be difficult, for the heritability of the character seems to be high. The Santa Gertrudis breed, for instance, has a very short and glossy coat, yet this breed is substantially only three-eighths Brahman; moreover, it transmits shortness of coat very strongly to its half-bred progeny when crossed with European breeds. Practical breeders also affirm that within the European beef breeds the "tropical" type coats run in families. As further evidence of the heritability of the character, Bonsma's (1949) success in establishing strains of short-coated Herefords and Shorthorns in South Africa may be mentioned, while Turner and Schleger (1960) from their Rockhampton, Queensland, data, estimate heritability of coat score at the high level of 0.63.

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HIGH TEMPERATURE AS A LIMITING FACTOR IN THE REPRODUCTION OF SHEEP AND CATTLE

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Abstract – For full fertility bulls and rams must preserve an abdominotesticular temperature gradient of at least 5° to 7° C. The scrotum facilitates this by conduction, sweating and specialised vasculature. Elevation of testis temperature impairs spermatogenesis. Recommendations for avoiding high temperature male infertility include: use of heat-tolerant breeds; avoiding rams and bulls with a long, pendular scrotum; shearing rams (if shade is plentiful); selecting rams with little scrotal wool. High temperature also affects female reproduction, causing embryo resorption or birth of miniature young. Heat resistant breeds should be used and the hottest months avoided for the early part of pregnancy.

Zusammenfassung – Die Erhaltung der vollen Fruchtbarkeit beim Stier und beim Schafbock ist an das Vorhandensein eines Temperaturgefälles zwischen dem Rumpf und den Hoden von mindestens 5° – 7° C gebunden. Dieses Temperaturgefälle wird normalerweise gewährleistet durch trockene und feuchte Wärmeabgabe vom Hoden sowie durch eine spezielle Anordnung der Hodenblutgefässe. Eine Erhöhung der Hodentemperatur beeinträchtigt die Spermatogenese. Zur Verhinderung der temperaturbedingten Sterilität des männlichen Tieres werden empfohlen: Verwendung hitzetoleranter Rassen, Vermeidung von Böcken und Stieren mit einem langen, hängenden Hodensack, Scheren der Böcke (sofern Schatten vorhanden ist) und Auswahl von Böcken mit schwachbehaartem Hodensack. Beim weiblichen Tier verursacht hohe Temperatur Embryo-Resorption oder Geburt von Miniaturtieren. Auch hier sollten hitzetolerante Rassen verwendet werden und die erste Zeit der Trächtigkeit sollte nicht mit der heissesten Zeit des Jahres zusammenfallen.

Résumé – Afin que la fertilité des taureaux et des béliers soit la meilleure, le gradient thermique entre l'abdomen et les testicules doit être d'au moins 5 à 7° C. Ce gradient thermique est normalement obtenu par une émission calorique sèche ou humide au niveau des testicules, ainsi que par la disposition particulière des vaisseaux sanguins de ces dernières. Une élévation de la chaleur des testicules diminue la spermatogénèse. Afin d'empécher la stérilité due au manque de gradient thermique on conseille: d'utiliser des races à haute tolérance à la chaleur, d'éviter d'utiliser des taureaux et de béliers présentant un scrotum allongé et de tondre les béliers (s'il y a de l'ombre en suffisance) et de choisir ceux qui ont un scrotum peu poilu. Chez les femelles, les hautes températures provoquent la résorbtion des embryons ou la naissance de petits miniatures. Ici aussi, il est indiqué de sélectionner les races à haute tolérance à la chaleur et de ne pas faire correspondre les premiers temps de la gestation avec la période la plus chaude de l'année.

MALE FERTILITY

It is well known that high temperature is harmful to spermatogenesis in both the ram (Phillips and McKenzie. 1934; Gunn, Sanders and Granger, 1942) and the bull (Casady *et al.*, 1953). Obviously this has serious implications in countries where high temperatures prevail, and to avoid wastage through poor fertility from this cause, understanding is required of the physiological background of the problem, the degree of heating likely to precipitate the trouble, and the extent of breed or individual resistance to it.

Physiology

The scrotum serves a thermo-regulatory function. In some species it maintains the testes close to the body; in others the attachment is more pendulous. These differences are associated with abdomino-testicular temperature gradients which are believed to have an evolutionary significance (Cowles, 1958). Sheep and cattle both have a pendulous type of scrotum in accordance with which their testicular temperature is normally well below body temperature. The gradient is of the order of 5°–7° C in the ram (Harrison and Weiner, 1949; Waites and Moule, 1961) and probably at least as great in the bull, as judged by the temperature of semen at time of ejaculation (Calaprice and Dello Joio, 1960).

Sheep and cattle are equipped in three main ways to preserve this temperature gradient which, it will be seen, is essential to their fertility:

(a) By reflex control of the dartos and cremaster muscles the scrotum is contracted and the testes brought into close apposition with the body in cold weather, while under hot conditions these muscles relax placing the testes further from the body and increasing the surface area of the scrotum (Phillips and McKenzie, 1934; Beakley and Findlay, 1955).

(b) The evaporation of sweat secreted from the sweat glands of the scrotum promotes the cooling of this organ. Even in the sheep, which has a general sweating rate only about one fifth that of cattle (c.f. Brook and Short, 1960; McDowell *et al.* 1961) scrotal sweating is significant, and under hot-room conditions has been found to increase from 0.6 g per scrotum per hour at air temperature 27° C to 1.5 g at 41° C (Moule, 1951).

(c) The arterial vascular pattern of the testis is such as to ensure the nearest equality of temperature between the scrotum and the whole mass of testis tissue; moreover the close relation of the pampiniform plexus of veins to the highly convoluted testicular artery in the spermatic cord, is well adapted to bring about precooling of the arterial blood flow to the testis. (Harrison, 1949; Harrison and Weiner, 1949).

Temperature

Phillips and McKenzie (1934), from their observations on rams' scrota, concluded that as environmental temperature increases from 6° to 24° C, the dartos muscle becomes increasingly relaxed and the testes correspondingly more pendulous; above 24° C they found no further relaxation. Beakley and Findlay (1955) by indirect methods made a similar finding in young bulls, though they named 30° C as the probable temperature beyond which there was in their experiments no further relaxation. Apparently it is at about these temperatures that scrotal sweating starts and evaporative cooling assumes importance taking over, as it were, from simple heat exchange by conduction. The significance of this change is of course all the greater as environmental temperature approaches, and finally passes, scrotal temperature.

Clearly, then, at temperatures beyond 24° to 30° C the ability of rams and bulls to preserve their abdomino-testicular gradient of 5° to 7° C will depend increasingly on their scrotal sweating ability and on efficiency of evaporation, though general competence in preserving normal body temperature will also assist.

Elimination of the abdomino-testicular gradient completely disrupts spermatogenesis. This is conclusively shown by the fact that cryptorchid testes produce no sperm. But even short-term heating of less degree may be harmful. Thus reduction of the gradient by 5° C using scrotal insulation for as little as 24 hr (Glover, 1955) resulted in the sudden appearance 17 to 24 days later of tailless spermatozoa in the semen. Glover interpreted this as interference with spermatogenesis rather than damage to fully formed spermatozoa.

Dutt and Hamm (1957) have reported that after hot-room exposure to 32° C for a week, Southdown rams suffered seminal degeneration which these workers attributed to a 1.7° C rise in average body temperature of the rams during the week of exposure. The decline in semen quality became evident in the second week following treatment and was most severe in the fifth week. By the eighth week semen quality had returned to normal.

Breed and Individual Differences

In so far as ability to preserve normal body temperature assists maintenance of the abdomino-testicular gradient, those breeds having the best overall heat tolerance should also be the most fertile under hot conditions. This appears to be so in practice with cattle, Bonsma, Sholtz and Badenhorst (1940) having found Africander cattle to be superior in heat tolerance and fertility to British beef breeds in South Africa, while Bhatnagar (1958) has reported a similar dual superiority of Indian dairy breeds over Jerseys imported from New Zealand to India. Evidence is harder to acquire with sheep since light as well as temperature is involved in the so-called "summer sterility" of rams. However, on both counts (heat tolerance superiority and minimal photoperiodic sensitivity) Merino rams should be more fertile than rams of the British breeds in summer-time in hot regions.

Dutt and Hamm (1957) found under hot-room conditions that the shearing of rams, by lowering body temperature, improved semen quality as compared with unshorn animals. However, under field conditions unless adequate shade is available, at least 4 cm of wool is necessary to protect sheep adequately from direct solar heating (Parer, 1963).

With regard to scrotal insulation it would seem advantageous on general grounds to discriminate in hot climates against rams with heavily woolled scrota (Webster, 1952). In Glover's (1955) experiments, however, Romney Marsh rams with abundant wool on their scrota were less affected by artificial insulation than Suffolks almost devoid of scrotal wool. This suggests that the Romneys may have developed some compensatory cooling mechanism. Badenhorst (1951) infers that exaggerated lengthening of the scrotum, which he regards as detrimental, might derive from this cause (excess wool). He found Merino rams with short scrota to be more efficient than those with very long scrota. Kirby and Harrison (1954) have reported similarly for cattle. Symington (1960), too, has found increase in scrotal pendulance to be related inversely to ability to maintain normal body temperature in German Merino, Blackhead Persian and Native rams in Rhodesia.

FEMALE FERTILITY

Sheep

Although high temperature seems to have little or no effect on either the incidence of oestrus or the length of the di-oestrous interval (Yeates, 1953), experiments by the same worker leave no doubt that over-heating may be harmful to the normal course of gestation. Thus pregnant Romney Marsh ewes subjected for 6 hr daily to temperatures of 40.5° C exhibited a severe reduction in the number of ewes actually lambing, while those which did lamb produced dwarfed lambs, much below the normal in birth weight. The degree of failure depends on the duration and severity of the ewes' exposure to heat; also on breed and possibly nutrition. That breed is involved is shown by extension of experiments to Merinos (Yeates 1956, 1958). Ewes of this breed proved much more resistant, no doubt owing to their greater heat tolerance. However, higher temperatures (44.5° C) and a lowered plane of nutrition produced an effect similar to that of heat alone on Romneys and far more pronounced than simple undernutrition in a control group of Merinos.

According to Dutt, Ellington and Carlton (1959) high temperature in the premating and immediate post-mating period is specially likely to cause embryo loss is sheep. From their experiments they infer that tubal eggs are particularly susceptible to heat, or that heat possibly interferes with sperm livability or transport in the Fallopian tubes.

Poor lambing percentage and the depressed birth weight of lambs following summer gestation is a field problem in tropical Queensland (Moule, 1954) and all evidence points to it being an effect of high air temperature on the ewe. In South Africa, too, Merinos are frequently mated in early summer, hence the high incidence of embryonic death reported by Hunter (1959) may well be a heat effect. In Trangie, N.S.W., an area marginal for heat, the problem was associated with a particularly hot summer (Morley, 1954).

Cattle

There is evidence of gestational heat susceptibility among cattle, too, though apparently the effect is restricted to those individuals which are poorly heat adapted. Bonsma (1949) found that poorly adapted cows had "puny" calves (20 per cent below normal weight) when service was in August to September in Northern Transvaal. The same cows when bred in March to April were unaffected. The calves of well adapted animals showed no weight difference as between seasons of mating.

Cause

The mechanism by which heat produces either embryonic resorption or foetal dwarfing is obscure, though some interesting leads have been obtained. Shah (1956), from egg transfer experiments in rabbits, has shown that the problem of resorption is due not to the direct effect of heat on the embryos, but to impairment of the maternal tissues. The egg transfer approach has also been used by Alliston and Ulberg (1961) with sheep. Quite recently, Ryle (1963) has provided evidence supporting the idea that the resorption may be due to thyroxine insufficiency.

Recommendations

Even if the problem proves to be one of decreased thyroid activity, thyroxine therapy would seem to be contra-indicated under high temperature conditions. Accordingly, it is suggested that stock should be used which are well adapted to heat; and, if possible, to ensure that the early part of pregnancy does not coincide with the very hot time of year.

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PHYSIOLOGICAL THERMONEUTRALITY ZONES OF CATTLE

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Abstract – The range of thermoneutral zone is approximately the same for Holstein, Jersey, Brown Swiss and Brahman cattle, but the boundaries or the critical temperatures vary considerably with the breed. An index or expression for the physiological thermoneutral zone, with distinction of cold, and heat indices for these breeds have been shown. These studies have emphasized the need for further investigations on the thermoneutral zones and the physiological basis for these zones for cattle.

Zusammenfassung – Der Bereich der thermoneutralen Zone ist bei Holstein-, Jersey-, Brown Swiss- und Brahman-Rindern von annährend gleicher Grösse. Dagegen sind die Grenzen dieser Zone, die sogenannten kritischen Temperaturen, je nach der Rasse verschieden. Als ein Ausdruck für diese kritischen Temperaturen bei den verschiedenen Rassen wurde ein Kälte-Index und ein Wärme-Index entwickelt. Es wird auf die Notwendigkeit hingewiesen, weitere Untersuchungen durchzuführen über die thermoneutrale Zone beim Rind sowie über die sie beeinflussenden physiologischen Grössen.

Résumé – L'amplitude de la zone thermiquement neutre est pour ainsi dire la même pour le bétail des races Holstein, Jersey, brune de Suisse et Brahman. Les limites de cette zone, c'est à dire les températures critiques, sont par contre différentes de race en race. On a établi pour chacune d'elles un index de froid et un index de chaud exprimant ces températures critiques. On attire l'attention des chercheurs sur la nécessité d'entreprendre d'autres recherches sur les zones thermiquement neutres du bétail ainsi que sur les grandeurs physiologiques qu'elles influencent.

INTRODUCTION

Zones of thermoneutrality are dependent upon the functioning of homeothermic and thermo-regulatory mechanisms. These mechanisms include the temperature regulation centers in the hypothalamus and the neuro-endocrine system and related physiological factors. The physiological adjustment of warm blooded animals to environmental temperature and other related climatic factors. e.g. temperature, humidity, radiation, are believed to be influenced by many factors including age, acclimation, size, species and nutritional state.

The "zone of neutrality" is the environmental temperature where heat production is minimal at normal body temperatures.

The term "comfort zone" is used widely for cattle and believed by Brody (1948) to be similar to the physiologist's thermoneutrality zone. The "comfort zone" as derived by Thom (1959) is based on responses or expression of many people to various temperature humidity conditions. There is a human physiological basis for use of this term (Sohar *et al.*, 1962) and for cattle (Johnson *et al.*, 1962).

Within the thermoneutrality and comfort zone the animal does not activate thermo-regulatory physical and chemical devices. The environmental temperature is perfectly adjusted to keep the body temperature normal and the animal apparently feels neither hot nor cold.

In general, temperature regulating mechanisms as well as the various mechanisms concerned in each physiological reaction may be controlled by the same central mechanisms as suggested by Keller's (1938) original hypothesis concerning heat regulation. It has been suggested recently that hypothalamic mechanisms which controlled heat loss and heat production were intermingled diffusely in the anterior hypothalamus and the posterior lobe. Also, the peripheral receptors may play an important role in the cold weather, but do not play any role in case of high temperature (Benzinger *et al.*, 1961). It has been further suggested that there are internal efferent signals within the hypothalamus in response to high temperature. More recently, the role of hypothalamie temperatures in controlling the feed and water intake (Andersson and Larsson, 1961), and thyroid responses of ruminants (Andersson *et al.*, 1962) are being actively investigated.

These data suggest some of the basic neuro-endocrine mechanisms concerned with homeothermy. In this paper we propose to use the term physiological thermoneutrality to describe the neutral environmental zone in which heat producing or dissipating mechanisms are not activated or depressed. These data and conclusions are based on responses of four breeds of lactating cattle (fed *ad libitum*) to controlled laboratory conditions. Exposures to the various temperatures were approximately of two weeks or more duration.

Heat production, Heat Dissipation and Related Functions as Affected by Environmental Temperature

Heat production has been studied extensively by using the mask method which is identical with the Benedict–Roth–Collins "basal metabolism" apparatus used in hospitals, except for size and mask type. This type of mask or sample collection has been developed by Yousef *et al.* (1963) and Hahn *et al.* (1963).

Food consumption was found to be depressed by high environmental temperature (Brobeck, 1948; Brody, 1945, 1948; Ragsdale *et al.*, 1948, 1951; Kibler and Brody, 1949, 1950; Worstell and Brody, 1953); thus, resulting in a decrease in metabolism and other productive processes, which lessened the amount of heat produced (Kibler and Brody, 1956; Kibler, 1960, 1962) by the animal.

Dale and Brody (1954) showed that increasing air temperature depressed the CO_2 combining capacity to a greater extent in the large Holsteins, than in the smaller Jerseys and Brahmans, and at 80° F the maximal decline in CO_2 capacity was affected in all breeds, so that breed differences in their reaction disappeared. Also, they indicated that blood pH increased with increase in thermal stress, apparently caused by the pulmonary over-ventilation associated with heat stress. The concentration of ketone bodies in the urine remained within the normal range, showing the tendency to increase with increasing thermal stress.

As is generally known, thyroxine is associated directly and indirectly with O_2 consumption, other factors, such as feed consumption, milk production, thyroid activity (Johnson *et al.*, 1957, 1958, 1959, 1960) and recently it has been shown that glucocorticoids (Bergeman and Johnson, 1963) adjust to changes in body temperature regulation. That is, the increasing difficulties encountered in heat elimination with increasing environmental temperature reduces the rate of heat production. Kibler and Brody (1950) studied the influence of temperatures of 5° to 95° F on evaporative cooling from the respiratory and exterior body surfaces in these two breeds (Jersey and Holstein), and they concluded that: (a) uneventful rises in respiratory vaporization with rising temperature 5° to 95° F, amount to a moisture vaporization range of 12 to 53 g/m^2 hr and account for 4 to 30 per cent of the total heat dissipation; and (b) between 5° and 60° F, the outer surface vaporization was of about the same order as the respiratory vaporization but between 50° and 80° F the surface vaporization increased four-fold to a near maximal value of about 80 cal/m^2 hr.

Exposure of cattle to temperatures above 65° F caused a decrease in heat production (Kibler and Brody, 1949). At that time these results were unexpected because they contradict the Van't Hoff-Arrhenius rule to the effect that increasing the temperature of a physiochemical system increases its reaction rate. However, more recent data by Kibler (1960) showed that short term exposures to hot temperatures accelerated heat production.

These differences may be explained by the fact that animals which were exposed suddenly to high temperatures did not have sufficient time to diminish feed intake, milk production etc.

The rate of non-evaporative cooling (sum of convective, radiative, and conductive cooling) follows Newton's Law of Cooling. In cold weather heat dissipation is mostly by non-evaporation cooling; in hot weather mostly by evaporative cooling. Moisture vaporization is an efficient method of cooling because of its high latent heat of vaporization which ranges from about 580 cal/kg at 22° C to 640 cal/kg at 33° C (Hardy, 1949).

Other Environmental Factors that Influence the Thermoneutral Zone

Increasing atmospheric humidity at temperature levels from 75° to 100° F depressed heat production in all cows at 85° F, depressed the respiratory vaporization rate at above 85° F especially in the Holstein cattle, and depressed vaporization rate from the skin or outer surface at temperatures from 75° to 95° F. Thompson *et al.* (1953) studied the effect of humidity on insensible weight loss, total vaporized moisture, and surface temperature in cattle, and they demonstrated that at 12° and 40° F air temperature there was no indication that increasing humidity affected vaporization rate. At temperatures of 75°, 85° and 95° F there was noticeable depression of vaporization with increasing humidity. Also at 85° F and above, skin and hair temperature of the cows were increased, some on increasing relative humidity; at 12° and 40° F, however, there was no significant effect of relative humidity on skin temperature. The influence of wind has been studied (Thompson *et al.*, 1954) on the effects of low, medium, and high air velocities (0.4, 4 to 6, and 8 to 9 mph.) at 18°, 50°, 65°, 80°, and 95° F on total evaporative cooling (and insensible weight loss) and on surface temperature (hair and skin) of lactating Holstein and Jersey and non-lactating Jersey animals.

When data were plotted against environmental temperature, vaporization at low air velocity gradually increased with increasing temperatures from 18° to 65°, then more rapidly to 80° F when maximum vaporization is reached. But when vaporization at high velocity is similarly plotted the rapid increase in vaporization begins nearer 80° F and continues up to 95° F. The effect of increasing air velocity on evaporative cooling and surface temperature was non-linear and greater in increasing the wind from 0.4 to 5 than from 5 to 9 mph.

Kibler and Brody (1954) indicated that at 45° F air temperature, increasing radiation did not appreciably affect the heat production of Holstein and Jersey cattle. At 70° and 80° air temperature, the mean heat production rate in Jersey cows was 12–14 per cent lower at maximum radiation of 500 kcal/m^2 hr than at "zero" radiation. The data for Holstein cows showed parallel decreases in heat production with increasing radiation amounting to 26 per cent at 70° F and 9 per cent at 80° F air temperature as the intensity of radiation increased. Kibler and Brody (1954) concluded that the metabolic weight loss (the excess of CO_2 and CH_4 production over O_2 consumption) tended to decrease in the Holstein group at high level of radiation at 70° to 80° F. The vaporization from the respiratory tract and skin, and therefore the total vaporization, increased with rising intensity of radiation. With this information it may be said that the animals showed as great or greater heat strain at 70° F air temperature with full radiation (500 kcal/m^2) hr than at 80° F without radiation.

In summary, at cold temperatures, increasing air velocity should raise the critical temperature, and radiation should lower it. At higher temperatures increasing radiation and humidity will lower the critical temperatures, and air velocity will raise it.

MATERIALS AND METHODS

The following data were obtained primarily from numerous experiments on cattle in the Missouri Climatic Laboratory, a laboratory which was designed to study the complex climatic factors and effects on milk production associated physiological reactions.

In this laboratory 12 cows may be maintained on experiment at a time. The data represent the animals response at each chamber temperature level. Values, in most cases, except extreme temperatures were obtained after two or more weeks exposure. The rate of heat production was computed from the rate of O_2 consumption, CO_2 production, pulmonary ventilation and respiratory vaporization as measured by open-circuit mask method; respiration rate by counting flank movements; total vaporized moisture as estimated by insensible weight loss; ^{131}PBI/total ^{131}I, blood CO_2 combining capacity, ascorbic acid, and creatinine by standard laboratory procedures as described in Environmental Physiology. (Environmental Series Research Bulletin 515 by Worstell and Brody, 1953).

RESULTS AND DISCUSSION

Considerable data have been collected for four breeds; Holstein, Jersey, Brown Swiss, and Brahman and have been used as a basis for the general expression for the physiological factors that are concerned with the zone of thermoneutrality. From Fig. 1 one may conclude that the range of the thermoneutral zone is approximately

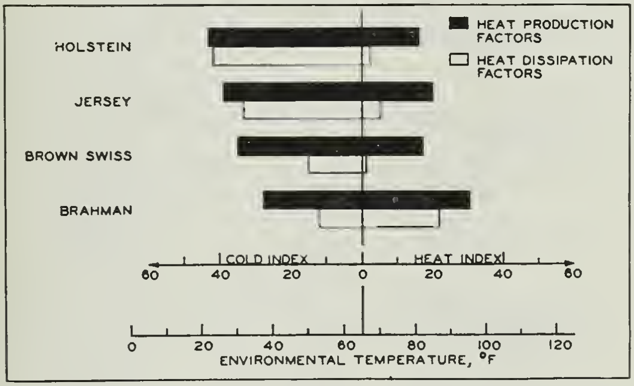

FIG. 1. Physiological thermoneutral zones (av. environmental temperature range in which physiological parameters do not change). Lactating cows were on *ad libitum* feeding conditions. 65° F is used as a reference temperature to estimate magnitude of cold or heat thermoneutral index. Factors measured and considered to be related to heat production are: Feed consumption, milk production, pulse rate, body weight, CO_2 combining capacity, blood ascorbic acid, PBI^{131}/total I^{131} ratio. Factors measured and considered to be related to heat dissipation are: Respiration rate, total vaporized moisture, respiratory vaporization, pulmonary vaporization, blood creatinine, per cent evaporization cooling/heat production

the same for these four breeds i.e. 59°, 59°, 52° and 58° F for Holstein, Brown Swiss, Jersey, and Brahman lactating cattle respectively. However, it should be emphasized that the boundaries or critical temperatures for this zone are different for each breed. The boundaries are 21°–80° F; 26°–85° F; 30°–82° F and 37°–95° F for Holstein, Jersey, Brown Swiss, and Brahman respectively. The differences in critical temperatures are due to factors associated with heat production and heat dissipation factors that are in general concerned with physical and chemical heat regulatory mechanisms. These differences may be due to the efficiency of the breed in the heat production and dissipation mechanisms. Within this range of temperature the animal should theoretically have an optimal level of physiological functions.

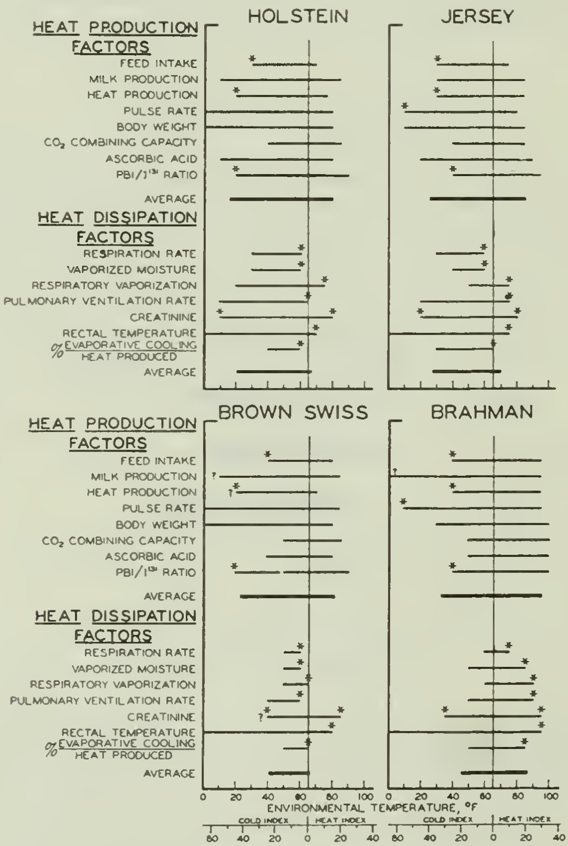

FIG. 2. Thermoneutral Zones: Average environmental temperature range in which measured physiological parameters do not change, (increase or decrease)

Using 65° F as a base value and comparing the critical temperatures above and below this temperature, one arrives at an expression of the critical cold or heat index.

Heat regulatory dissipation and related factors were separated as described in Figs. 1 and 2.

The cold indices based on heat production and associated factors are 43, 39, 31, and 28 respectively for Holstein, Brown Swiss, Jersey, and Brahman. The heat index values are 16, 19, 17, and 31 respectively.

It is readily apparent that other physiological factors may be used in these indices, however, other data were not available for this wide range of temperatures. It is hoped that future research in this area will clarify and modify these conclusions.

In this paper we have used the term thermoneutral zone in more or less an unorthodox manner, particularly since these data presented are on lactating animals exposed for periods of weeks to various temperatures receiving feed and water *ad libitum*.

Fasting data on cattle, lactating and dry, are needed at various environmental temperatures. These would probably shift the thermoneutral zones toward the higher temperatures.

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THERMOREGULATORY RESPONSES OF THE DEHYDRATED OX TO HEAT EXPOSURE AND TO REHYDRATION

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RESTRICTION of water for 4 days changed the responses of oxen to heat during a 4-hr exposure to an atmosphere of 40° C dry bulb and 32° C wet bulb temperature: Respiratory rate was depressed and skin evaporation delayed; rectal, skin and subcutaneous temperatures rose to higher levels. These findings suggested the possibility that in the dehydrated state the thermal thresholds for panting and sweating were increased. Rehydration with cold water caused the body temperatures to fall by about 1.7° C and immediately depressed the respiratory rate from 130 to 40 respirations/min. Rehydration with water at body temperature had no effect on body temperature but increased respiratory rate. The implications of these findings are discussed.

RESPONSES OF CATTLE TO WATER RESTRICTION IN A TEMPERATE AND IN A WARM ENVIRONMENT

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STEERS that had been deprived of drinking water for 4 days in an environment of 15° C showed decreases in hay dry matter intake (71 per cent), faeces excretion (−73 per cent), urine excretion (−45 per cent), insensible weight loss (−59 per cent), body weight (−11 per cent), heat production (−18 per cent), respiratory minute volume (−42 per cent), plasma potassium concentration (−5 per cent) and in urinary potassium output (−59 per cent). The treatment also caused increases in haematocrit (19 per cent), in the concentrations of plasma total solids (18 per cent), blood urea (200 per cent), plasma sodium (13 per cent), plasma chloride (10 per cent) and in the output of urinary sodium (500 per cent). Depriving the same animals of water for only 2 days in an environment of 40° C caused qualitatively similar changes in most of the quantities investigated. The implications of these findings are discussed.

A MODERN RESPIRATION CALORIMETER

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THE ventilation system of a Benzinger-type gradient layer direct calorimeter, suitable for animals up to 100 kg liveweight, has been modified to permit continuous automatic analysis of the out-going airstream by commercially available instruments. Re-circulation of any desired fraction of the airstream increases the O_2 decrement and the concentration of CO_2 and CH_4 while the humidity is maintained at a pre-selected level. O_2 concentration is measured by a paramagnetic analyser while infrared instruments are used to determine CO_2 and CH_4. Gas analysis records are plotted on a roll-chart which also carries the calorimetric data.

THE EFFECT OF FEEDING LEVEL ON VARIOUS COMPONENTS OF HEAT LOSS IN SHEEP

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THE daily heat loss of a 5-year-old Scottish Blackface ewe was measured at various levels of energy intake by means of a gradient layer direct calorimeter. Total heat output, automatically sub-divided into sensible and insensible losses by this instrument, was further partitioned into the cutaneous and respiratory evaporative components by a technique which permitted independent ventilation of head and body while leaving the animal some freedom of movement. The results of this work show that the variation in radiation, convection and cutaneous water loss was surprisingly small. About 90 per cent of the increase in heat loss between starvation and twice maintenance feeding level was due to increased respiratory activity.

ATTRIBUTES OF THE PELAGE IN MAMMALS RELEVANT TO ITS THERMOREGULATORY ROLE, ESPECIALLY IN THE SHEEP

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THE importance was stressed of considering the integument as a whole when assessing the thermoregulatory role of the pelage in mammals. Highly relevant in this respect were the hair follicles, the tubular glands, the acinous glands, and the smooth musculature. Taking the sheep as an example, the author gave ranges of a large number of characters of the skin and pelage. In view of the great variation shown he demanded a precise definition of these structures, particularly when making inter-species comparisons.

THE PLANE OF NUTRITION AND SOME RESPONSES TO SUSTAINED CLIMATIC STRESS IN SHEEP

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EXPERIMENTS were reported in which sheep of two breeds on three planes of nutrition were exposed to four different types of heat stress. It was shown that the sheep on the highest plane of nutrition suffered the highest strain and that humid heat was more stressful than dry heat.

ABSORPTION OF SOLAR RADIATION BY THE COAT OF DOMESTIC ANIMALS

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A METHOD is described for measuring the absorption of solar radiation from cattle coats. A comparative study with 20 cows showed that Brown Swiss cows in Poland at an altitude of 120 m tended to have a smaller absorption than Brown Swiss cows in Switzerland at an altitude of 1600 m. Results obtained from 7 horses are also given.

RADIATIVE HEAT LOSS IN COW SHEDS

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THE cooling rates of two thermostatically controlled spheres ("Frigorimeter"), one black, one nickel covered, were determined within a cow shed. In one series of experiments the cows were present, in another series they were absent. The contribution of infrared radiation to the cooling rate was estimated to be at least 40 per cent.

THE EFFECT OF FOOD INTAKE ON THERMOREGULATION

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The complexity of the relationship that exists between food intake, thermoregulation, coat character, physical exercise, and growth rate in cattle living in hot countries was emphasized. While recognizing the calorigenic effect of food intake the author maintained that the extra heat generated could easily be dissipated provided the animal had a short, sleek coat.

DETRIMENTAL EFFECTS OF HIGH AMBIENT TEMPERATURE ON FERTILITY AND EARLY EMBRYO SURVIVAL IN SHEEP

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Exposure of ewes to an environmental temperature of 32° C raised rectal temperature by 1.7° C on average. This significantly depressed the percentage of ova fertilised and increased the number of morphologically abnormal ova. Heating the ewes before or at the time of breeding stopped them completely from lambing. Heating them at 1, 3, 5, or 8 days after breeding resulted in lambing percentages of 20, 35, 40 and 70 per cent, indicating that the sheep zygote is most sensitive to high temperature during the initial stages of cleavage, i.e. while still in the oviduct. The results suggest that sexual differences in fertility of livestock may in part be due to changes in the female reproductive system and not entirely due to changes in the fertility of the male.

INFLUENCE OF THE PREOPTIC-ANTERIOR HYPOTHALAMIC REGION ON THERMOREGULATION AND ALIMENTATION

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LOCAL cooling of the preoptic/anterior hypothalamic region of unanesthetized goats was performed by water perfusion of chronically implanted silver thermodes. In an environment of 18° to 21° C, brain chilling promptly elicited cold defense mechanisms (peripheral vasoconstriction, increased levels of plasma thyroxine, elevated excretion of adrenal catecholamines) resulting in development of a marked core hyperthermia (41.0° to 41.8° C). Shivering, however, did not occur, or was of brief duration. When central cooling was continued for three days, goats failed to drink water up to 50 hr, and thereafter did not drink enough to restore the water deficit incurred until cooling was terminated. Food intake, in contrast, was stimulated, or maintained, despite the condition of dehydration and core hyperthermia. It is suggested that the thermosensitive region of the diencephalon normally maintains a brake on cold defense mechanisms, and, further, exerts a thermostatic influence on food and water intake.

THE EFFECT OF ENVIRONMENTAL TEMPERATURE ON SKIN TEMPERATURE AND HEAT LOSS IN THE YOUNG PIG

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THE relationship between environmental temperature and skin temperature on the trunk of the two month old pig between 25° and 35° C is similar to that in nude man below his critical temperature. Between 25° and $-5°$ C there appears to be some mechanism which tends to oppose the fall in skin temperature. At $-5°$ C the temperature on the tip of the ear fluctuates widely. The thermal circulation index increases between 25° and 30° C and the index also increases at $-5°$ C. The rate of increase in non-evaporative heat-loss from the trunk with fall in dry bulb temperature is similar to that in nude man and the closely clipped sheep. Water loss from the skin is very low and even at 35° C when body temperature increases cutaneous water loss can be accounted for by passive diffusion through the skin.

EFFECTS OF THE THERMAL ENVIRONMENT ON THE FERTILITY OF BULLS

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Using fans on an experimental group of bulls kept indoors at temperatures between 18° and 25° C significantly increased semen quality (motility and survival time) over that of a control group. It was concluded that the thermal environment should be characterised in terms of atmospheric cooling power, as measured for instance with the Kata-thermometer, and not in terms of air temperature. Libido, sexual behaviour and semen quality of bulls were found to be influenced by weather conditions. Atmospheric pressure and ozone content of the air seemed to be of particular importance.

CLIMATIC STRESS RESPONSES AND INDICES IN DOMESTIC ANIMALS

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RESPONSES of six breeds of cattle to heat were reported (Fig. 1.) In most of the physiological parameters investigated significant changes occured when body temperature had risen above normal by about (0.8° C). In this state the animals were regarded as being stressed. Heat tolerance differed between breeds as well as within breeds. Two Holstein cows of similar production potential were shown to display striking differences in heat tolerance. It was suggested that future investigations of stress in cattle should give consideration to the stress concept of Hans Selye.

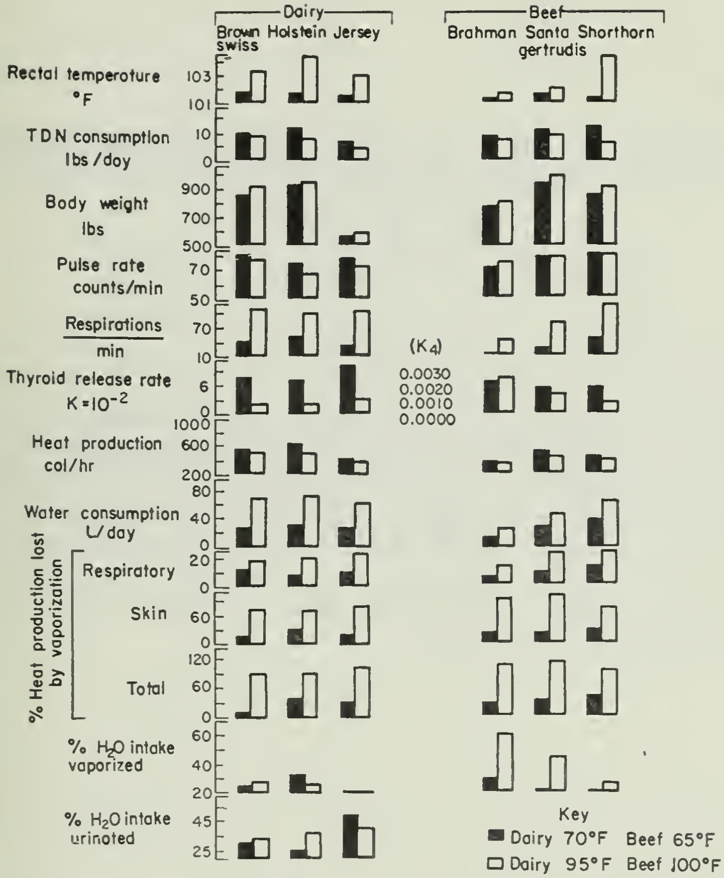

Fig. 1. A physiological comparison of animal responses to heat by six breeds of cattle. Holstein and Shorthorn animals are usually less heat tolerant than Brahman heifers as shown in the above charts. Santa Gertrudis appear to have successfully combined the heat tolerance Brahman characteristics with the productive features of the Shorthorn.

(Animals were reared at 50° F (control) and 80° F (experimental) temperatures and were approximately 12–15 months of age.)

THE EFFECT OF AIR MOVEMENT, AMBIENT TEMPERATURE AND SOLAR RADIATION ON THE INTERNAL AND EXTERNAL INSULATION OF SHEEP

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INTERNAL insulation of sheep (calculated from rectal temperature, skin temperature and heat production) was unaffected by air movement and ambient temperature, provided vasoconstriction had taken place. External insulation (joint insulation of the coat and the air interface) increased linearily with increasing fleece length over the range of 5 to 50 mm; it decreased with increasing air movement and was also affected by solar radiation. Heat production of sheep kept out-of-doors was much higher than that of sheep kept under comparable conditions of ambient temperature and confinement in a calorimeter.

CLIMATIC STRESS INDICES IN DOMESTIC ANIMALS*

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STRESS was defined as the magnitude of the external conditions operating upon the animal and tending to displace it from a state of normal equilibrium. Strain was defined as the displacement from normal, occurring in the animal as a result of the application of a stress. In man heat strain has successfully been expressed as the ratio between applied heat stress and maximum skin evaporation. It was suggested to apply this concept to heat strain in animals by making appropriate allowances for respiratory evaporation and for the presence of the hair coat.

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THE ENVIRONMENTAL TEMPERATURE PREFERRED BY THE YOUNG PIG

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PIGS up to six weeks of age were introduced for short periods either singly or in groups of five, into a thermocline comprising four communicating chambers and with a mean temperature range of 26° to 36° C. The mean preferred temperature was close to 30° C, both for single pigs and for groups, with the exception of pigs less than one day old where the corresponding value was 32° C.

CRITERIA FOR ESTIMATING FERTILITY IN CATTLE FOR STATISTICAL ANALYSIS

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FERTILITY is considered to be the most sensitive indicator of the response of cattle to environmental stimuli. As a measure of fertility in the female animal the "Umrinderungsquote" is proposed. This is the number of unsuccessful inseminations as a percentage of the total inseminations. It is shown that with increasing light in the cowhouse, expressed as proportion of window area to floor area, the "Umrinderungsquote" decreases, i.e. fertility increases.

EFFECT OF CLIMATIC FACTORS ON THE METABOLISM OF NUTRIENTS IN YOUNG GOATS

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DIGESTABILITY trials were performed on 8 young goats during the four seasons of the year. Air temperatures ranged from 12° to 41° C; vapour pressures from 8 to 32 mm Hg. It was found that the ratio of water consumption to dry matter intake increased with increasing temperature. Water output, as a percentage of water intake, had a minimum in summer and a maximum in winter. The digestability of dry matter, protein, fat and total carbohydrates showed a maximum in winter. These seasonally induced changes were greater than the changes due to age.

STILLBIRTH AND DEFECTS OF CALVES AT BIRTH IN RELATION TO SEASON

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There is evidence in the literature that reproduction in farm animals is affected by season. An analysis of the occurrence of stillbirth and various defects of calves at birth was made, using data compiled from the Dutch cattle herdbooks and from the records of artificial insemination centres. From the total number of calvings the frequency of occurrence of each of the defects was obtained. This frequency was compared with the calculated expected frequency. Some of the characters investigated, notably schistosomum reflexum, epitheliogenesis imperfecta and the occurrence of red and white Friesian calves failed to show a significant relation to season. The frequencies of the three lethal factors—hydrops, mummification and amputated bulldog calves—were found to be related to the season of birth. There was, however, the complication that the length of gestation was irregular. The occurrence of spastic paralysis was higher in autumn-born than in spring-born calves, while that of hernia umbillicalis was lowest at the end of the year. In both instances there was a significant relation to the season of conception, and the pattern was attributed to non-climatic seasonal factors such as feeding, management and the period of gestation. The percentage of stillborn calves was found to increase in autumn and to decrease in early spring. This pattern was considered to reflect the influence of the climate on various reproductive functions, such as ovarian activity, silent heat and length of gestation. It was thought that the hormonal balance, which is known to be affected by the seasonal changes of the climate, was an important factor in bringing about these changes in reproduction leading to stillbirth.

SUMMARY REPORT

W. BIANCA

INTRODUCTION

Veterinary biometeorology deals with the effects of weather and climate on domestic animals. Research on this subject uses two main lines of approach: The field worker describes the effects of the natural meteorological environment on animal performance; the laboratory worker tries to elucidate the underlying physiological mechanisms by studying animal responses to the controlled environments within climatic rooms. This diversity in approach sometimes makes it difficult for the field worker and the laboratory worker to understand one another. It should be recognized, however, that both strive towards the same goal and that their functions are complementary. Progress in veterinary biometeorology should, therefore, be best achieved by a balanced integration of field and laboratory work. It is hoped that the sessions of this working group which included both these approaches, have been useful.

ORGANIZATION

The sessions of the working group on veterinary biometeorology took place on five afternoons and lasted for a total of seventeen hours. There were 28 speakers from 10 countries who presented 34 short papers. Three of these papers were read in German, all the others in English.

In view of the very wide range of subjects covered by veterinary biometeorology, an attempt was made to find an optimal compromise between an approach which was too extensive and one which was too intensive. This had been done by selecting 11 topics which were thought to occupy strategic positions in the field of veterinary biometeorology and which would stimulate discussion. The number of papers presented in each of these sections ranged from 1 to 5; some of the sections suffered from late cancellations of contributions.

Since about one-third of the papers presented were not intended for publication in the Proceedings of the Congress, a brief description will be given in this report of the gist of all the papers presented. Of the various contributions made in the discussions only those will be considered which appear of major importance.

METHODS, TECHNIQUES AND INSTRUMENTS USED IN EVALUATING THE EFFECTS OF WEATHER AND CLIMATE ON ANIMALS

This was an obvious first choice of a topic for discussion, since research in animal biometeorology, becoming more refined, demands the development of new techniques and new tools.

Such a new tool is the gradient layer direct calorimeter. First, Stewart in a theoretical approach discussed the thermoregulatory responses of the animal as a biological analogue to an automatic feed back control system, and emphasized the importance of using direct calorimetry for the study of thermoregulation of large farm animals. Pullar then gave a detailed description of a modern Benzinger-type gradient layer direct calorimeter which had been developed and built at the Rowett Institute. It can accommodate animals up to 100 kg in weight and has recently been modified to permit continuous automatic analysis of the outgoing air stream by commercially available instruments. Total heat loss over a 24-hr period can be measured with an accuracy of about ± 15 kcal.

Moving from calorimetry, a method completely restricted to indoor work, to a method with at least a potential application for out-of-door work, McLean described a mask method for measuring exchange of respiratory gases in cattle. The striking feature of this method was that spot measurements of heat production could be made over a sampling period as short as 2 min. Extending the sampling period beyond 2 min did not appreciably improve the repeatability of the method (which was about 7 per cent). Under field conditions the shortness of the sampling time would have the practical advantage of keeping the size of a Douglas bag small. As possible drawbacks of the method, effects of the mask on respiratory rate had to be take into consideration.

The discussion moved from indoor work completely to outdoor work when Gloyne, a meteorologist, raised the problem of how to achieve consistency between the physical and the biological measurements in field studies with livestock. He came to the conclusion that the response times of various physiological parameters (skin temperature, heat production, etc.) were such as to permit the use of conventional meteorological apparatus. Sampling meteorological variables at intervals over hourly periods could provide biologically meaningful and therefore useful information for field studies with livestock. Gloyne also presented data from a field survey on the effect of the ground contour on the surface wind and gave critical slope angles for the breakaway of airstreams.

In the ensuing discussion Lee pointed out two main limitations of the cup anemometer. It is insensitive to air movements below about 2 to 3 mph and is orientated more to the horizontal than to the vertical component. Mount pointed out that the low sensitivity of wind meters is a serious limitation to the assessment of the climatic environment in pig houses, where it is important to detect low rates of air movement as draughts. Mount then described an instrument for measuring the climatic environment in farrowing houses, which takes into account air temperature, air movement and radiation from heating lamps. The instrument, which essentially consists of three different types of thermometers one of which contains a heating coil, is sensitive to changes in air speed up to 200 ft/min which is the range required for measurements in pig houses.

Much of the discussion in this section showed a clear trend towards a closer collaboration between the meteorologist and the biologist, a trend which should be pursued in future.

THE THERMOREGULATORY SIGNIFICANCE OF THE HAIR COAT OF MAMMALS

Approaching the animal from the outside, the various structures and functional features of the hair coat and the skin, which of course, constitute the interface between the animal and its climatic environment, were discussed.

Dealing first with the impact of a cold environment, Joyce discussed how air velocity and solar radiation aggravate or alleviate cold stress and how this is modified by the depth of the fleece. External insulation of the sheep (defined as the joint insulation of the air interface and the coat) was shown to increase linearily with fleece length over the range 5–50 mm. In assessing the effect of solar radiation on the external insulation of sheep, differences in reflection values (albedo) of long discoloured and short white fleece have to be taken into consideration. From the experiments it was evident that sheep kept out of doors have maintenance requirements much greater than those determined in the thermoneutral conditions of the calorimeter, a finding which emphasizes the importance of field studies under natural conditions. In the discussion, Mount presented figures on the insulative properties of the sparse hair of the baby pig. Removal of the coat during the first 10 days following birth reduced the thermal insulation by about 15 per cent. Shaving at an age of 2–3 weeks did not produce consistent changes, probably because tissue insulation had increased owing to deposition of subcutaneous fat (the new-born has no subcutaneous fat).

All the following papers dealt with the hair coat in relation to a hot environment. Yeats drew attention to the double role played by the hair coat or fleece in hot environments: interference with evaporative and convective cooling from the skin and protection against heat gain from intense solar radiation. Which of these two functions is more important obviously depends on the type of heat load (hot humid air, or radiant heat from the sun) and on whether sweating or panting is the predominant mechanism of evaporative cooling. According to recent investigations coat colour does not seem to play a dominant role in heat tolerance. Despite the clearcut differences in the ability of different coloured coats to reflect solar radiation, greater emphasis is placed now on sweating ability, glossiness and shortness of the coat. Shedding of the coat, formerly believed to be exclusively regulated by day-length, has been shown to depend at least in part also on environmental temperature, possibly involving the action of thyroxine. There is evidence of distinct breed differences in shedding: Seasonal coat changes are most pronounced in high latitude breeds (such as the Scottish beef breeds), and practically absent in equatorial breeds (such as the Ankole breed). Ankole cattle transferred to London Zoo failed to grow a thick winter coat, apparently lacking the genetic capacity to do so.

In a following paper Dowling reported on field experiments performed with cattle in the semi-arid region of Queensland. Tolerance to heat or to a combination of heat and exercise depended: (1) on the coat cover, short "summer" coats being associated with high heat tolerance, long "winter" coats with a low heat tolerance, (2) on the sweating ability, as suggested by experiments performed at different air movements, as well as by experiments involving artificial wetting of the coat and the use of plastic overcoats. Comparing cattle with man, Dowling maintained that cattle may be at least as heat tolerant as man provided they have fully adapted to heat by shedding their coats.

In the discussions following the papers by Yeates and Dowling it was further confirmed that shedding was dependent not only on the photoperiod, but also on ambient temperature. McDowell found that exposure of cattle in a climatic room to a temperature of 32° C had different effects on winter and on summer adapted animals. In winter adapted animals the heat exposure produced two sheddings, a first one after 5 weeks, a second one after 8 weeks; in summer adapted animals it caused an arrest of hair growth but no shedding. In the experience of Bonsma cattle had two seasonal periods of hair shedding, one in spring and one in autumn. Preliminary field observations with cattle by Stegenga showed that hair growth under a cover (outer layer: canvas, inner layer: jute) tended to be accelerated compared to hair growth of uncovered control animals.

The well-known fact that hair growth is a very complex function depending on a multitude of factors, climatic as well as non-climatic ones, received further support. Gale reported that chronic local cooling of the anterior hypothalamus of non-anaesthetized goats produced a noticeable augmentation of hair growth in summer months and that lesions in the median eminence of the tuber cinereum resulted in marked hair loss, diabetes insipidus, and blockage of thyroid activation after cold exposure. That hair growth is also under hormonal control was indicated by the observations of Bonsma who found that pregnant heifers shed their hair sooner than non-pregnant animals. The association of a woolly coat with sterility, frequently found in European type cattle in the tropics, confirmed also by the work of Pagot in West Africa, likewise suggests a causal relationship, but one which goes in the other direction, the causal chain being: woolly coat – poor thermoregulation – hyperthermia – sterility.

In spite of the dependence of coat character on many environmental factors there seems to be good evidence to indicate that coat character has a high heritability which makes selection for coat character a worthwhile procedure. The selection in hot countries of cattle having a short smooth coat and a well pigmented skin – postulated by Bonsma many years ago – has again been found useful under conditions in French West Africa by Pagot.

In a final paper in this section Carter made the point that in assessing the thermo-regulatory role of the pelage in mammals the integument as a whole must be considered. Taking as an example the sheep – a species being distributed over most climatic regions of the world – he gave ranges for a large number of characters of the skin and pelage. In view of the great variation, he demanded a precise definition of these structures, particularly when making inter-species comparisons. There followed a discussion on the terminology of skin glands. Findlay said that sweat glands of cattle should not be called apocrine, since there was no evidence that they secreted in a necrobiotic fashion. Their mode of function was still obscure and experiments involving iontophoresis should be treated with reserve since iontophoresis may block the sebaceous glands. Carter drew attention to the apparent paradox of the seal (a marine mammal) having "sweat glands". There might, however, be a need for evaporative cooling in the seal basking in the sun on a warm rock.

THE PHYSIOLOGY OF THERMAL PANTING

Only one paper, entitled "the cardiovascular responses of the ox *(Bos taurus)* to hyperthermia", was read in this section. In this paper Whittow pointed out that an increase in respiratory rate, blood pressure, heart rate and in the skin temperatures of the extremities could be produced either by warming the skin alone or by localized heating of the hypothalamus. Under severe heat stress, however, thermal, polypnoea was superseded by slower deeper breathing (second-phase breathing) and although the work of the heart was increased under these conditions there was no evidence of circulatory failure, cardiac output and blood pressure being higher than normal.

In the discussion McDowell suggested that second-phase breathing might be an indication of fatigue. Whittow considered this unlikely because: (a) the work of breathing is probably higher during second-phase breathing than during thermal polypnoea, and (b) second-phase breathing can be produced at will by repeated localized heating of the hypothalamus when the animal is already mildly hyperthermic. Lee pointed out also that since second-phase breathing is associated with an increased respiratory minute volume there could be no question of fatigue. Yeates asked what benefit an animal achieves by increasing its cutaneous blood flow when the environmental temperature is equal to the deep body temperature. Whittow replied that cattle under hot conditions lose most of the heat that they produce by evaporation of moisture from the skin. One function of the increased blood flow to the skin would be the supply of water for vaporization. If the activity of the sweat glands is involved in the moisture vaporization from the skin and if the sweat glands are under humoral control, variations in cutaneous blood flow must have a controlling influence on sweat gland activity.

WATER EXCHANGE OF ANIMALS IN VARIOUS CLIMATES

In a first paper, McDowell showed that the water consumption of cattle continuously exposed to an atmosphere of 32° C for 16–30 weeks underwent marked changes: a rapid rise to a peak during the first few weeks, followed by a fall to a level twice or more the normal level. Body temperature behaved in a similar fashion. Water consumption and body temperature were highly correlated (0.7). Throughout the exposure hair coat depth decreased. These findings clearly stressed the importance of long-term studies. Regarding water loss the speaker emphasized the thermoregulatory advantage of evaporation of water over the loss of water in urine, faeces and saliva. Skin evaporation was effected predominantly through sweat gland activity. The heritability estimate for sweating was quoted to approach 40 per cent, an encouragingly high figure which would warrant selection for this character.

The following two papers dealt with water exchange of dehydrated steers. Findlay reporting on an experiment performed jointly with McLean and Bianca, showed that heat alone, i.e. an atmosphere of 40° C dry bulb and 20° C wet bulb temperature produced a state of mild heat stress in the animals but did not upset their water balance. However, withholding water from the animals for 4 days in a temperate environment (15° C) or 2 days in a hot environment (40° C) affected them profoundly: voluntary food intake decreased and there was a trend for metabolic rate to decline. Water output from all three sources – evaporation, faeces and urine – declined. Haematological changes suggested a hypertonic contraction of the plasma volume. When at the end of the dehydration period water was offered *ad libitum*, large quantities of water were consumed in a few minutes. This produced shivering, but only in a temperate environment. In a warm environment shivering was probably suppressed by warm stimuli from the periphery.

Bianca found that deprivation of water for 4 days (in a temperate environment) changed the responses of steers to heat stress. When exposed for 4 hr to 40.0° C dry bulb and 32.5° C wet bulb temperature respiratory rate was depressed and the onset of sweating was delayed. Probably as a direct result of a reduced evaporation from the respiratory tract and the skin, body temperature rose to a higher level. These findings suggested the possibility that in the dehydrated state the thermal thresholds for panting and sweating were raised. When the steers, still exposed to heat, were offered water *ad libitum* they drank up to 60 l. within about 4 min. This caused body temperatures to fall by 1.7° C, and immediately depressed respiratory rate from 130 to 40 respirations/min. Drinking the same amount of warm water (40° C) had no effect on body temperature but unexpectedly caused respiratory rate to rise to 180 respirations/min.

In the discussion Johnson pointed out that dry cows responded to heat stress differently from lactating cows. Dry cows always increased their water consumption, whereas lactating cows did not necessarily do so. He then enquired whether in dehydration studies one could not empty the rumen in order to avoid the complication arising from the presence of an unknown amount of water in the rumen. In the opinion of Fisher emptying the rumen of cattle completely was not possible without serious risks to the animal. Fisher further drew attention to the complex interrelationship of dehydration, food intake and salivation. He thought that the finding that the amount by which the jugular haematocrit exceeded the mammary haematocrit was greater in the lactating than in the dry cow, indicated that in the lactating cow more water was extracted from the blood of the head than in the dry cow. This might be due to a higher rate of salivation in the lactating cow (which of course, also has a higher food intake).

Discussing diuresis, the authors of the papers on dehydration stated that after the sudden ingestion of large amounts of water there was no increase in urine output. Obviously, one would expect diuresis only to occur under a positive water load but even then, as observed by Fisher, diuresis in cattle appeared later than expected, suggesting that water moved through the body more slowly in cattle than it did in the dog and man. Whittow pointed out that the increase in the sodium/potassium ratio in the plasma of the dehydrated animals suggested an increased secretion of aldosterone from the adrenal cortex.

In a subsequent paper Pagot compared the water requirements of two bovine species living in the tropical climate of Mali under conditions of extensive grazing: N'Dama, representing *Bos Taurus*, and Zebu, representing *Bos Indicus*. He found that during the rainy season, which was relatively cool and humid, increases in air temperature raised water consumption, whereas increases in humidity depressed it. During the hot dry season increases in air temperature affected water consumption only a little, but increases in humidity raised it. The reaction to humidity changes was much more pronounced in the Zebus than in the N'Damas, from which it was concluded that the N'Damas were more tolerant to high humidity than the Zebus. In agreement with this, the geographical distribution of the two species showed the N'Damas to live in the humid zones, the Zebus in the dry zones. However, it was also found that the Zebus had lower values for rectal temperature, heart rate and respiratory frequency, than the N'Damas.

Foster read a paper on the "composition of the secretion from the eccrine sweat glands of the cat's foot pad". He discussed in detail the concentrations of various electrolytes and their interrelationships.

INDICES OF CLIMATIC STRESS IN DOMESTIC ANIMALS

Lee made a most useful contribution when in his opening paper he made a clear distinction between the terms stress and strain—two terms which are frequently used in a loose sense. He defined stress as "the magnitude of the external conditions operating upon the animal and tending to displace it from a state of normal equilibrium", and strain as "the displacement from normal occurring in the animal as a result of the application of a stress". Lee then suggested that heat strain should be expressed as a ratio between applied heat stress and the maximum rate of evaporation from the animal. This concept had originally been developed for man but it seemed that it could be applied also to cattle if an appropriate term for respiratory evaporation was incorporated in the equation. An example of this was presented.

In the ensuing discussion Bianca remarked that the principle on which the index was based was sound enough but that the procedure was rather involved, since it necessitated the determination of the ceiling response for each individual animal. He wondered whether there was any known relationship of the proposed index to a single more easily measured parameter such as body temperature, which would allow a shortcut to be made. After all, body temperature, the resultant of all heat gain and heat loss processes, should reflect the efficiency of evaporation from the animal.

Under the heading "climatic stress responses and indices in domestic animals" Johnson presented data on numerous physiological responses of 6 breeds of cattle to heat. All the results were obtained after an acclimatization period of about 2 weeks. In most of the functions significant changes occurred when body temperature was elevated by about 0.8° C above normal. In this state cattle were regarded as being "stressed". The breed comparison clearly demonstrated the low heat tolerance of Holstein and Shorthorn animals and the high heat tolerance of Brahman and Santa Gertrudis animals. The latter represented a successful combination of high heat tolerance and high productive capacity inherited from the respective Brahman and Shorthorn ancestry. Most heartening from the breeders' point of view was the finding that individual variation in heat tolerance within one breed could be very considerable. Two Holstein cows of a similar production potential displayed striking differences in heat tolerance.

Inevitably the pros and cons of Hans Selye's concept of stress were brought into the discussion which, as usual, generated more heat than illumination. It is a pity that generally Selye's concept seems to be either completely rejected or completely accepted, often without very good foundation for either. Johnson made the common sense suggestion that it was more important to recognize that a stress problem did exist and to find some guide line for the use of this word, than to quibble about details in Selye's concept.

Stephan lighted the problem from a different angle. He was not interested in an index of climatic stress as an end in itself but as a means for making an early prediction of an animal's capacity for production. He exposed cows to heat (35° C, 27 g H_2O/m^3 air) as well as to cold ($-8°$ C), took blood samples at intervals of about 2 to 16 hr and determined (amongst other parameters) haematocrit, blood sugar, total serum protein and blood specific conductivity. By comparing these results with the individual milk yields, he came to the tentative conclusion that the response to climatic stress developed more rapidly and was more intense in the high producing than in the low producing cows. In reply to a question by Gales, Stephan stated that at an air temperature of $-8°$ C, rectal temperatures of his cows were not depressed.

Bonsma thought that short exposures of animals in climatic rooms to a hot atmosphere gave little information about their overall adaptability to a tropical or sub-tropical environment. He maintained that the productive performance of the animals, in particular their efficiency of reproduction, was the best criterion of their total reaction to a total environment.

Finally the discussion centred on the stressing agent itself: the climate. The meteorologist Gloyne asked the questions: (1) which meteorological variables were needed to specify the climatic environment, and (2) how these variables could be assembled into an index which was meaningful to the animal husbandry man. He also emphasized the importance of sequences of weather in relation to stress and recovery.

FOOD INTAKE AND THERMOREGULATION

Dowling in his opening paper emphasized the very complex relationship that exists between food intake, thermoregulation, coat character, physical exercise and growth rate. While recognizing the effect of food intake on heat production he maintained that the extra heat generated could easily be dissipated even in a hot environment, provided the animal had a short, sleek coat. Such animals when exposed to heat were able to eat much, walk long distances and gain weight rapidly.

In the discussion Bonsma commented on the "melanin stars" shown by one of the bulls on the slides, which in his opinion indicated a high vascularity of the skin, and thus a desirable structure in a hot environment. Bianca added that "melanin stars" had also been described by Dürst, in fattened steers.

Carter then reported on experiments in which sheep of two breeds (Corriedales and Camden Park Merinos) on three planes of nutrition were exposed to four different types of heat stress. It was shown that the sheep on the highest plane of nutrition suffered the highest strain and that humid heat was more stressful than dry heat.

In a following paper McDowell showed that the level of food intake largely determined the response of cattle to heat stress. When dry and lactating Holstein cows were fed according to their requirements (which were 2 to 3 times higher in the lactating than in the dry cows) the lactating cows responded to heat exposure (32° to 38° C) with a marked rise in body temperature, whereas the dry cows showed hardly any response at all. When, in a second trial, dry cows were fed at the same level as their lactating counterparts, the difference in heat response became very much smaller. When, in a third trial, dry cows and cows in their 6th month of lactation were fed at the same level, there was virtually no difference in their heat response. A difference developed only at the highest environmental temperatures. A diet with a high fibre content tended to depress heat tolerance and milk yield. Thus, avoiding high fibre diets by the use of appropriate husbandry methods (right type of forages, right time of harvesting; etc.) was a means by which the heat stress could be lessened and production increased.

In a final paper in this section Gale dealt with some of the mechanisms involved in the control of body temperature and of alimentation. Local cooling of the preoptic-anterior hypothalamic region of the brain of non-anaesthetized goats living in an environment around 20° C elicited cold defence mechanisms which led to a marked core hyperthermia. When cooling was continued for several days the animals did not drink, which resulted in a state of dehydration. In spite of dehydration and elevated core temperature food intake was maintained or even increased. These findings suggested that this region of the brain normally maintains a brake on cold defence mechanisms and that it exerts a thermostatic influence on food and water intake.

THE ZONE OF THERMONEUTRALITY IN DOMESTIC ANIMALS

Heitman reporting on experiments conducted jointly with Bond and Kelly, seemed to have doubts about the very existence of a thermal neutral zone in pigs, at least in fully fed pigs. Using a climatic room that had been modified to serve as a calorimeter he determined the total heat loss of hogs of different body weights at air temperatures ranging from 4° to 38° C. The results were presented as curves derived from regression equations. These curves did not show distinct zones of thermoneutrality. The point of minimum heat loss was around 27° C in the 23 kg hogs and around 33° C in the 91 kg hogs, which meant that with rising body weight this point shifted to the warm side. This finding was unexpected, since earlier work by the same author had shown that the maximum value for weight gain shifted to the cold side with rising body weight. Furthermore, the temperatures for minimum heat loss were higher than the temperatures for maximum weight gain.

In the discussion McLean said that it was not permissible to disprove the existence of a zone of thermoneutrality on the basis of the fitted curves, since the choice of a parabolic curve (as a best fit for the data) already precluded the existence of such a zone. It was felt that it would have been helpful if the original data had been given as well.

In the following paper Stewart discussed the theoretical basis of animal thermoneutrality, by treating it as a thermodynamic rate process. He pointed out that in a system at constant temperature the degradation of free energy was a measure of the inefficiency of the system and that the creation of entropy was the criterion of such a degradation. Thermoneutrality was then defined as the state in which energy dissipation or entropy production was minimum.

Finally Johnson read a paper by himself and Yousef on physiological thermoneutrality zones of cattle. He had determined for 4 breeds of lactating cattle fed *ad libitum*, the range of ambient temperature within which body functions were neither activated nor depressed. As criteria, over a dozen physiological parameters were used, some relating to heat production, some to heat loss. Regarding the average behaviour of the parameters involved in heat production, it was found that the thermal zone in which no changes occurred, had about the same magnitude for Holstein, Jersey, Brown Swiss and Brahman cows, namely 29° to 33° C. However, the position of this zone differed from breed to breed. In the Holsteins the zone was shifted towards the cold side, in the Brahmans towards the warm side. Jerseys and Brown Swiss cows were intermediate. The two end points of each zone (the critical temperatures) were then expressed as deviations from 18.3° C and termed cold index and heat index respectively. These index figures allowed breed distinctions to be made.

In the discussion Bianca drew attention to the fact that many of the parameters investigated were functionally interrelated, and that some of them were obviously of greater importance for thermoregulation than others. He suggested that it might be useful to multiply each of the parameters with a weighting factor that was in proportion to its actual influence. Otherwise the average might give a distorted picture. Whittow commented that there were instances in which in response to cold the heat production increased before the insulation had reached its maximum.

HEAT AND COLD AS LIMITING FACTORS IN ANIMAL PRODUCTION

Bonsma, instead of reading his paper on heat as a limiting factor in animal production, showed a series of colour slides which illustrated his main points in a most palatable fashion. They particularly underlined Bonsma's thesis, based on a 20 years experience in selecting, breeding and handling cattle in the tropics, that the texture of the hair coat is the most important single morphological characteristic that determines the heat tolerance of cattle. Animals possessing a smooth woolly coat were poor producers. This was found to be true even for Africaners. Woolly coated Africaner crossbreds (a rare mutant) showed a low growth rate. On the other hand, Herefords which had a smooth glossy coat performed relatively well in the heat. In Bonsma's opinion animals in a hot environment will show a significant drop in production long before signs of heat strain (notably increase in respiratory activity and body temperature), are evident. This would mean that production was not only the final measure of heat tolerance but perhaps the most sensitive as well. However, he recognized the advantages of an actual test and thought that serological tests might warrant further investigation.

Next, Sommer reported on an investigation on the effects of weather on milk yield in cows. He compared daily milk yields of 24 cows over one complete lactation with 6 successive weather phases, as defined by Ungeheuer. It was found that milk yield tended to be elevated in the "settled" phases 2 and 6, and to be depressed in the "unsettled" phases 3 and 4. The sensitivity to these weather phases varied from animal to animal, and seemed to be associated with characters important in breeding. The over-sensitive cows produced calves that were inferior to those produced by the less-sensitive cows. Thus the degree of weather sensitivity might develop into an aid for predicting an animal's breeding value.

In the discussions various speakers emphasized the importance of separating the effects of weather from those of nutrition, management, and other non-meteorological factors. Stegenga also mentioned the delay in the response to weather changes. In his experience changes in milk yield followed changes in weather with a delay of about 12 hr.

EFFECTS OF WEATHER AND CLIMATE ON REPRODUCTION

Yeates critically reviewed the present state of knowledge regarding the effects of high ambient temperature on the reproduction of sheep and cattle. He emphasized the importance of three main points: understanding of the physiological background of the problem, knowledge of the magnitude of heat load likely to precipitate the trouble, and knowledge of the inherent resistance of breeds and individuals. In the male, fertility depended on the preservation of an adequate temperature gradient between the testes and the trunk. Below an ambient temperature of about 24° to 30° C a gradient of the order of 5° to 7° C could normally be upheld by means of various mechanisms. Above this temperature, however, spermatogenesis became disrupted. In the female, high temperatures did not seem to have much effect on oestrous, but interfered with the normal course of gestation. The pre-mating and the immediate post-mating periods were considered to be the critical ones. Overheating in these periods frequently resulted in the production of dwarfed animals. The mechanism leading to foetal dwarfing or to embryonic resorption has not yet been fully elucidated. Recent work suggests thyroxine insufficiency as a possible causative factor.

Discussing this paper, Bonsma pointed out that *Bos Indicus* and *Bos Taurus* differed markedly with regard to the vascularity of the scrotum. Furthermore, there was evidence that a bull with a very pendulous scrotum had a lowered fertility. The birth of miniature calves from heat stressed cows was a frequent occurrence under South African conditions.

Next, Müller showed that the fertility of cows improved with increasing light in the cow house. As a measure of fertility he used the "Umrinderungsquote", i.e. the number of unsuccessful inseminations as a percentage of the total inseminations. The author also advocated the use of "mass-statistical" methods in fertility studies with cattle.

A last paper in this section read by Stegenga, dealt with stillbirths and defects of calves at birth in relation to season. His figures were based on records from the Dutch cattle herdbooks and A. I. centres. It was found that spastic paralysis of the hind leg in calves occurred more frequently in animals born in autumn than in animals born in summer. The percentage of still-born calves was highest in autumn. The three lethal characters – hydrops, mummification and amputated plus bulldog calves – showed a significant relation to season. There was, however, the complication that the length of gestation of these calves is variable. The author then discussed the question whether such defects were due to climate *per se* or to other factors exhibiting seasonal fluctuations, particularly feeding and management. Regarding the physiological mechanisms directly responsible for the observed defects, seasonal fluctuations in hormonal balance were considered to be of importance.

BEHAVIOURAL THERMOREGULATION

Mount, reporting on the environmental temperature preferred by the young pig, described an arrangement of four communicating chambers in which mean temperatures were kept in the range 26° to 36° C. Pigs up to six weeks of age which were introduced into this "thermocline" for short periods either singly or in groups of five were found to prefer a temperature close to 30° C. Pigs less than one day old, preferred a temperature of 32° C.

THERMOREGULATION AND AGE

In this final section consideration was given to the reactions of young animals to a "hostile" environment. Ingram reported on the effect of environmental temperature on skin temperature and heat loss in the young pig. In an environment between 25° and 35° C the skin temperature on the trunk of two months old pigs behaved in much the same way as the skin temperature of nude man below his critical temperature. Between 25° and 30° C and also at 5° C the thermal circulation index showed an increase. Non-evaporative heat loss from the trunk declined with falling dry bulb temperature at a rate which was similar to that in nude man and the closely clipped sheep. Water loss from the skin was so low that it could be accounted for by passive diffusion through the skin.

In a following paper Blatteis dealt with the complex interrelationship of catecholamines, hypoxia and the metabolic response to cold in new-born rabbits. When new-born rabbits were given a low oxygen mixture (10 per cent O_2 in N_2) to breathe, the increase in oxygen consumption in response to cold (25° C) was suppressed. Furthermore, low oxygen breathing reduced the metabolic response to intravenous infusions of noradrenaline and of isoprenaline in a cold as well as in a thermoneutral environment. Hypoxia did not, however, affect the metabolic action of adrenaline, in either environment. These results indicated that the response of oxygen consumption to cold, to hypoxia and to catacholamines does not represent a straightforward relationship. It was suggested that heat production in the newborn is achieved by a combination of glycolysis and fatty acid oxidation. There was possibly a gradual conversion from uneconomical glycolysis to calorigenically more efficient fatty acid oxidation.

CONCLUSIONS

From the reports and the ensuing discussions the following general conclusions may be drawn. The study of heat exchange of the animal with its thermal environment has made great progress and is in the process of being further refined by the advent of direct calorimetry. At the same time, there is a certain trend to move the experimental animal from the "sheltered" environment of the calorimeter into the field, in order to include in the investigation also those climatic variables which can not easily be simulated indoors. This seemingly paradoxical situation merely shows that indoor as well as outdoor work is required, and that for a full understanding, the problem may have to undergo several passages in both directions between the natural outdoor environment and the controlled indoor environment.

It has been made abundantly clear, that in cattle a short sleek, glossy coat is associated with high heat tolerance, and a long, woolly, dull coat with low heat tolerance. However, there still remains the vexed question: is an animal heat intolerant because it has a woolly coat, or has it a woolly coat because it is heat intolerant owing to another condition which happens to produce a woolly coat? In other words, is the woolly coat the direct cause of heat intolerance, or is it merely one facet of a heat strain syndrome? Although there is good evidence for the existence of direct effects of the coat on heat tolerance, recent work has shown that a high heat stress may interfere with normal body functions, including endocrine balance, to such an extent as to cause changes in the hair coat. It seems important, that more work be done on the dependence of the hair coat on various body functions which are affected by climatic and other stressors, and that for this work the collaboration of the veterinary pathologist should be sought. In an even wider context it is necessary to disentangle the complex interrelationship of feeding, drinking, heat production, evaporative heat loss and coat type in the thermally stressed animal. To do this, carefully designed experiments are needed which allow each factor to be studied independently.

Terminology, once more, was found to be the potential cause of misunderstanding and confusion. Clear definitions of stress and strain as given in one of the contributions, are a first step in the right direction. Unambiguous definitions of skin glands, of adaptation, of acclimatization and other terms would be welcome.

The thorny problem of indices of climatic stress in animals has received attention, but it seems that the choice still lies between a method that measures in a simple and quick way a partial effect (e.g. body temperature) and a method that measures in a more complicated and time consuming way a more complete effect (e.g. the ratio between applied heat stress and the maximum rate of evaporation). Since neither of these two extreme solutions is completely satisfactory, future work will have to aim at an optimal compromise between them.

There is evidence to show that the weather can influence the organism, but it is still obscure which of the meteorological variables, singly or in combination, are responsible for such effects. In pursuing this problem further it seems important to consider not only the classical meteorological elements but also other component factors of the weather. This may best be done in collaboration with the meteorologist. Since a weather pattern can not be artificially simulated the problem might be approached by selective screening of weather elements, which would lead to a reduction in the number of potentially causative factors. Furthermore, it seems important to develop the studies in depth, i.e. to proceed from highly complex animal characters, such as milk yield, to the underlying physiological variables and mechanisms.