HEART ATTACK RARENESS
IN
THYROID-TREATED PATIENTS

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By

BRODA O. BARNES, Ph.D., M.D.

and

CHARLOTTE W. BARNES, M.A.

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PREFACE

THIS short treatise is written for both the layman and the scientist interested in preventing premature heart attacks. Hence, the language is simple, yet the facts are documented so that those desiring further information can pursue it. Heart attacks were unknown at the turn of the century, but they lead the list of the causes of death today. Present knowledge indicates that the carnage can be eliminated by close cooperation between the susceptible patient and the family doctor. For that reason it seems logical to discuss the modus operandi with both at the same time.

Autopsy studies leave little doubt that a low cholesterol diet will not prevent hardening of the arteries. One recent preliminary report suggests that patients on high polyunsaturated-fat diets may be more susceptible to cancer. It is apparent that previous suggestions of dietary alterations to prevent heart disease were premature and should be abandoned immediately until such alterations can be clearly demonstrated as safe and effective.

For almost a century evidence has been accumulating that thyroid deficiency is accompanied by atherosclerosis. It was accidentally discovered that premature heart attacks were rare in thyroid-treated patients. A thorough search of the literature revealed sufficient facts to support a rational theory associating hardening of the arteries with a lack of thyroid secretion. Time may supplant this theory with a better one; in the meantime, no harm will result from treating every patient having symptoms and other evidence of thyroid deficiency with physiological doses of thyroid hormone.

The major problem is to alert the patient as well as the physician to the early signs of thyroid deficiency. Since atherosclerosis begins in childhood, the family physician and the pediatrician hold the key to effective prophylaxis. Both of these physicians will find a tremendous amount of help with their problem-

youngsters if they suspect thyroid deficiency and treat them accordingly. The rest of the profession must realize that once thyroid deficiency has been recognized, therapy must be continued for life. Many heart attacks have occurred among those who have discontinued treatment.

A physician's first duty is the care of his patients, and the second is dissemination of new knowledge to his colleagues. For over ten years a concentrated program of the latter has been carried out. Publications in medical journals have given details of diagnosis and treatment. Scientific exhibits have been presented repeatedly at medical meetings from San Francisco to Boston, from New Orleans to Edmonton, Canada, and even in Holland as well as Austria. Numerous personal communications from other doctors likewise indicate that their patients have benefited by the new regime. Some authors are now beginning to publish similar results.

The authors are indebted to thousands of patients who have tolerated repeated absences from the office for medical meetings and the collection of data. They have been faithful in taking their medications, and now realize that in addition to the fringe benefits of improved health, most of them have escaped heart attacks befalling their friends. They have made a contribution to medical science.

Broda O. Barnes
Charlotte W. Barnes
2838 West Elizabeth
Fort Collins, Colorado 80521

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Chapter I

NOT ENVIRONMENT ALONE: A NEW POPULATION

"ARE you killing your husband?" screamed the headlines in the newspapers across the nation during the heat of the controversy over the causes of the rapidly rising rate of heart attacks. Such slogans are still thrown at the public by the more militant scientists who are convinced that cholesterol is the villain responsible for heart attacks, the leading killer of our time. Some have even berated government officials for not having passed legislation limiting the use of saturated fats.

This vociferous group is as convincing as the prosecution at a Perry Mason murder trial on T.V. However, in both cases the evidence against the alleged culprits is purely circumstantial. The solution of the mystery of heart attacks parallels the T.V. series very closely; several new suspicious characters are interrogated but found innocent. The original accused is exonerated, while an unexpected criminal is proven guilty beyond a shadow of doubt.

No one denies that heart attacks have risen from obscurity to the leading cause of death within the memory of millions. This is a radical change in death patterns. No doubt it is related either directly or indirectly to other radical changes which have taken place simultaneously.

Blaming saturated fats in the diet seems unjustified, since in reality these constituents for many people today are no higher than they were in the diet of our ancestors two hundred years ago. At that time most of the population lived on the farms where fresh dairy products and eggs could be produced economically at any season of the year. During the winter months meat could be preserved; fat meat was more palatable than tough, lean meat. During the summer months cured bacon and hams were supplemented with pork sausage fried down in lard.

Butter was used in abundance on the hot biscuits for breakfast

and on bread, which made up no small part of the diet. The milk was cooled for several hours in the old springhouse where a slow stream of water acted as a refrigerator. Thick cream was skimmed off the milk and was used generously on fresh or canned fruit. My grandfather used to say that even shoe-leather would be good with cream and sugar on it.

If a high cholesterol diet were as dangerous as alleged, all of the farmers would have died from heart attacks centuries ago, and the rest of the world would have starved to death. Will Rogers said that there was no substitute for horse-sense; this has surely been neglected in our reasoning about heart attacks.

The farmers were not dying from heart attacks one hundred years ago, nor were the doctors missing the diagnoses. As late as 1930 autopsy studies at Graz, Austria (to be discussed later), showed only one heart attack per 125 deaths. The diet of the Austrian has been similar to that in the United States. The farms are small and have cows, pigs, chickens, and beef animals. Dairy products are relatively cheap and consumed in large quantities. In 1970 the autopsies at Graz showed one heart attack for each 14 deaths, a rise of over 800 percent in thirty-five years. Later it will be shown that diet was not to blame for this rise.

Far more radical changes have occurred in the consumption of sugar. Some scientists feel that this has led to an elevation in the triglycerides of the blood which in turn causes heart attacks. Against such a theory is the rarity of heart attacks among populations subsisting largely on carbohydrates. A few investigators claim that there are different effects from consuming starch as opposed to sugar, but convincing evidence is lacking that increased sugar consumption is responsible for the changing death patterns.

Modern machinery has drastically reduced the amount of exercise necessary in routine work. The physical culture advocates blame our sedentary life for the rise in heart attacks. In my memory, the greatest enthusiast for clean living and vigorous exercise was my college professor of physical education. He was a near-perfect physical specimen, yet he had a heart attack before the age of 50.

Our beverage intake has changed dramatically over the years. Coffee has jumped; some feel that this may be a factor. Alcohol

continues to be a major health hazard; its effect on the arteries has not been settled. Soft drinks have become a billion-dollar industry; the effects of the artificial sweeteners require further study. Some of the minerals in our drinking water have been suspected of contributing to heart attacks.

Even the atmosphere we breathe has undergone tremendous changes in the last century. Pollution from industry and from the automobile sometimes makes the air dangerous to health. The carbon monoxide from the auto exhaust may contribute to hardening of the arteries in a manner to be described later. In the mind of the Surgeon General, cigarette smoke has been convicted of contributing to heart disease and many other illnesses. It is difficult to understand the reason that cigar and pipe smoke are considered safe since no difference in the smoke from the three sources has been clearly demonstrated.

Stress is alleged to be greater in modern society, yet this can be questioned since the government now aids in disasters from the womb to the tomb. Our forefathers had to solve their own problems; crises were as frequent in past centuries as they are today. Stress may aggravate or precipitate a heart attack, but it probably is not the underlying cause.

It is obvious that a multitude of changes have taken place in our environment. One or all may be contributing to the changing death patterns, but it is difficult to assess the relative value of each. It is impossible to run the crucial experiment of eliminating only one of the factors, and over a period of years to observe the effect on the incidence of heart attacks.

Perhaps the greatest change of all during the past two hundred years has been that in man himself. This possible factor has been neglected; all of the attention has been focused on changes in the environment. Two hundred years ago over half of the births died before reaching adult life. Beethoven was one of three survivors out of seven births. During his lifetime, premature deaths were due to infectious diseases rarely seen today. Epidemic diarrhea has been conquered, smallpox has all but disappeared, tuberculosis is far down the list, and millions of deaths among young people are prevented each year.

In the past, the senior citizens were composed of only those

who were resistant to infectious diseases; susceptible individuals died in childhood or early adult life. In the United States as late as 1931, tuberculosis was the leading cause of death in those between 15 and 39 years of age. Stopping the carnage from infectious diseases has resulted in senior citizens today being composed of two distinct groups of people: first, those who are resistant to infectious diseases, and second, those who are susceptible yet have escaped early death from infections as a result of modern medicine. At the present time the two groups are about equal in size.

The first group has not changed in its inheritance to the degenerative diseases of old age. Evolution has taken centuries for any noticeable alterations. Some of these individuals have died from one disease, some from another. A family tendency for a disease to predominate is often evident. For generations, cancer, hypertension with eventual heart failure, diabetes, strokes, and a host of other degenerative diseases have eliminated those surviving the ravages of infections.

The second group is composed of adults susceptible to infections but reaching old age because of immunizations and antibiotics; this group has never appeared in medical history of the past. For the first time, such individuals are eligible for degenerative diseases. They might be called "the new population" of adults in the twentieth century. Probably their greater longevity has not influenced their inheritance towards adult diseases. It is clear that their inheritance to infectious diseases was different from that of group one which was resistant to infectious diseases.

It should come as no surprise if members of "the new population" have a different inheritance to adult diseases, just as they had to infections. No new diseases have appeared during the radical change in death patterns of the twentieth century. Some degenerative diseases have shown a disproportionate rise while the infectious diseases have been declining. This balance between the decline in deaths from some diseases and the rise in others remains constant, since each birth leads to only one death.

The changes in the death patterns can be readily explained if one assumes that "the new population" contains a preponderance of individuals susceptible to three diseases, namely, emphysema,

lung cancer, and heart attacks. Evidence that this is true is rapidly accumulating. It has been demonstrated that patients with tuberculosis are twenty times more susceptible to lung cancer than are members of the general population (1). For years both tuberculosis and lung cancer were frequently found in the same patient, clearly showing that both diseases were competing for the life of the same individual. Emphysema has always been associated with infectious diseases.

Heart attacks were first associated with infectious diseases during World War II (2). There were 866 myocardial infarctions in men below the age of 40 among the 15,000,000 American military personnel. Only two important correlations were found: a family history of the disease in those afflicted, and a history of a previous pneumonia in the patient himself. Pneumonia is an indication of a low resistance to infectious diseases. Those individuals susceptible to infections are also more prone to heart attacks.

Thus it appears the "the new population" is more susceptible to a few diseases; this observation is a major factor in the radical change in death patterns in the twentieth century. Such a thesis is supported by the facts that no country with a high incidence of infectious diseases has had significant numbers of heart attacks, emphysema, and lung cancer. Conversely, no country has failed to see a rapid rise of these three afflictions as infectious diseases have been curtailed.

And now to conclude our murder mystery. In later chapters evidence will convict a thyroid deficiency as the culprit in premature heart attacks; cholesterol will be exonerated. A simple method of recognizing thyroid deficiency will be presented, followed by treatment which controls the incidence of early coronary deaths without alterations in diet or mode of living. It appears that the elimination of early deaths from infections has produced a "new population" more susceptible to heart attacks and other diseases giving a marked change in death patterns.

Chapter II

ARE HEART ATTACKS REALLY A MENACE?

THE evidence in the last chapter strongly indicates that the phenomenal rise in heart attacks and a few other diseases has resulted from modern medicine's reduction of premature deaths from infectious diseases. It is true that hardening of the arteries now accounts for one-third of the total deaths and that heart attacks lead the list. Does this mean that heart attacks, like the plague, have swept in to decimate mankind? Here again "horse sense" has been neglected.

What has happened to the nation's health during the past century as the death patterns have undergone the radical changes? The average survival has doubled! Does this sound as if civilization were doomed? Far from it! The rise of heart attacks is the greatest blessing in the history of medicine.

Heart attacks have not invaded all strata of society killing off the newborn, the children and the young adults. The routine autopsies at Graz, Austria, clearly show that there has been no decrease in the incidence of strokes, cancer, diabetes, hypertension, and other diseases of old age. In fact, each of these diseases has shown a slight increase, indicating that some of "the new population" escaping premature deaths from infections are adding to the various degenerative diseases.

The age at death for most degenerative diseases has changed very little during the twentieth century. Hence, the rise in longevity is due largely to the prevention of premature deaths from infectious diseases. It is "the new population" surviving into advanced years which has doubled the life span.

The Graz autopsies indicate that the average age of survival of patients dying with heart attacks, the leading cause of death, was 66 years in 1970. In 1930 at Graz, tuberculosis was the leading

cause of death, and the average age of survival for those individuals was 38 years. Clearly, the rise in heart attacks at the expense of tuberculosis cannot be looked upon as a catastrophe, but as a bonanza in disguise.

If heart attacks have risen as a natural consequence, why are some of our leading scientists screaming "wolf" today? They are overemphasizing the total number of heart attacks recorded without any regard for the ages at which they occur. Furthermore, those advocating changes in diet are not yet aware of any other approach to the problem. Their recent request for a billion dollar program to support a dubious, dietary theory indicates that all facts have not been considered.

Every effort is being expended to stop atherosclerosis or hardening of the arteries. Present evidence indicates that this may be a laudable ambition, but the odds are about as good as inventing perpetual motion. In addition, modern knowledge of pollution indicates that the fountain of youth would not be an asset; one of the worst pollutants would be an oversupply of man himself. Nature has maintained a reasonable balance in the past, and if aging were conquered, total birth control or legalized genocide would be the only alternatives.

Atherosclerosis is one of the oldest clinical demonstrations preserved in medical history. Some of the arteries from the occupants buried thousands of years ago in the Egyptian tombs clearly show this disease. Their diet may have contained an abundance of cholesterol, but certainly neither the automobile, the cigarette, nor other modern pollutants were present at that time. The mummies showing atherosclerosis were adults; the arteries probably represented aging as they do today. In view of the similarity to present lesions, it seems reasonable that a few individuals at that time may have died from heart attacks. However, this disease would have been rare due to the short life span of the early Egyptians.

Further evidence that modern society is not the sole cause of heart attacks dates back to some astute observations by Heberden over two hundred years ago. He was physician to the queen of England; hence, his qualifications were high, and his reputation undoubtedly attracted well-to-do patients in the older age groups.

He is not known in medical history for recognizing the symptoms of heart attacks, but rather has been immortalized by "Heberden's nodes," the enlargement of the joints in the fingers caused by rheumatism.

Heberden (3) reported 100 cases of acute chest pain on exertion, calling it "angina pectoris." He was aware that the pain disappeared promptly with rest and that sometimes a patient died suddenly without evident illness during an episode. In his series, men were afflicted far more frequently than women. In two hundred years very little has been added to the clinical picture of the condition we know as a "heart attack." Heberden did not have the scientific knowledge of the twentieth century; he did not realize that angina was due to a lack of blood supply to the heart muscle. He considered that the chest pain and sudden death were due to acute indigestion since the patient often vomited from pain.

It is apparent that atherosclerosis is not a new condition caused by modernization in the twentieth century but that it has been present for thousands of years. Likewise, heart attacks have been known for over two hundred years, long before dietary changes, cigarette smoking, sedentary living, and atmosphere pollution. There is no doubt that heart attacks have mushroomed in recent years, but "the new population" offers a better explanation than that of changes in the environment. This thesis will be expanded later. Atherosclerosis seems to be a natural process of aging. Our real goal should be the removal of the factors responsible for acceleration of aging among younger individuals.

Heart attacks are one of the more humane types of death. Often the person is leading an active, enjoyable life until shortly before his tragedy. The majority of heart attacks occur near the end of the normal life span. This is in contrast to death from tuberculosis which was the leading cause of death in the last century. In the latter, the young adult was usually the victim suffering prolonged disability with loss of appetite, strength, and weight. A racking cough, fever, drenching sweats, pain, and insomnia added to the misery of the patient who knew that death was inevitable. But when?

A patient with cancer would readily trade his lot for the risk of

a heart attack. It is not death that the patient fears in cancer but the agony of the death. Cancer ranks second as a cause of mortality today; a decrease in heart attacks permitting cancer to rise is not in our dreams. Can heart attacks be such a menace?

A glance at the age at which heart attacks occur throws considerable light on the subject. It is frustrating to read the occasional headlines that a promising, middle-aged man's career was suddenly terminated with a heart attack. This is news. But the hundreds of elderly victims beyond the average life span, whose deaths were sudden and relatively painless, are found only in the obituaries. Before abolishing heart attacks, it might be well to study the relative frequencies of the above occurrences.

According to the World Health Organization's vital statistics for 1966, the United States had 626,772 deaths from arteriosclerotic and degenerative heart diseases (4). This represented approximately one-third of the total deaths in the nation for that year. At first glance this appears to be a serious situation, yet the figures do not reveal the absence of thousands of deaths from infectious diseases which would have been present only a few years ago. The latter occurred at a much younger age.

A more realistic appraisal of our present situation can be made by comparing the above figures with some autopsy data collected by Ophuls (5) in San Francisco between 1900 and 1923. Among 3,000 consecutive deaths there were very few heart attacks; however, 50 percent of the total deaths occurred before the age of 45. The infectious diseases were decimating the population in a manner that heart attacks could never approach.

Looking at the age distribution of heart attacks in 1966, it is found that only 2.4 percent occurred before 45 years of age. In other words, this disease is confined largely to older people. In fact, 73 percent of the total were over 65 years of age. Thus, almost three-quarters of those dying from heart attacks had completed their economic contribution to retirement and were enjoying their savings supplemented by fringe benefits of social security and medicare!

The figures further reveal that many of these individuals had had several years of fruitful living as senior citizens. If the number of deaths are collected for five-year periods, it is found that the

largest number of all of the heart attacks occurred between ages 75 and 79. These facts do not indicate that heart attacks are a plague to be eliminated from our society. In fact, if a newborn had an opportunity of selecting his eventual cause of death, he could do no better than to choose atherosclerosis. No other disease permits its victim to live such a long and trouble-free life.

This does not mean that the 2.4 percent who die of heart attacks before the age of 45, or the additional 24 percent who succumb before 65, should be neglected. The scientists should concentrate not on the elimination of atherosclerosis but on the difference in susceptibility to the disease. Biological variation is universal in all species known; man is no exception in his response to atherosclerosis. If the progress of the disease could be delayed in those more susceptible, there would be no major problem from heart attacks. The following chapters indicate that the susceptible can be selected and that appropriate treatment will prevent the dreaded "premature" heart attacks seen in a relatively few young individuals. Then heart attacks will no longer be a menace.

Chapter III

CHOLESTEROL: FRIEND OR FOE?

FOR twenty years cholesterol was the topic of conversation at the dinner table, at the beauty parlor, or even over the back-yard fence. It has been surpassed recently by pollution. That does not mean that cholesterol has lost any of its importance. This compound is one of the fundamental building blocks in the animal kingdom; it must be taken "for better or for worse" even after medicare takes over. If all of it were removed from an animal, only a vegetable would remain; cholesterol is always found in the animal kingdom, but never in the plant world.

When the sperm from man goes forth in search of the egg from woman to create a new individual, each of these single, highly specialized cells carries its own supply of cholesterol. After union of these two cells, the cholesterol content of the mother's blood increases by about 50 percent; there is need for more of this substance since each of the billions of new cells constituting the fetus will contain cholesterol at term. If this compound were as toxic to the blood vessels as alleged, the fetus would have a heart attack before the baby saw the light of day. Such is not the case.

The importance of an adequate supply of cholesterol for the development of new tissue is clearly illustrated by the hen's egg. Of the common foods, eggs contain the highest concentration of this material. Nature has guaranteed a constant content of cholesterol in the egg; even feeding hens a diet free of cholesterol does not change the composition of the eggs. All of the cholesterol necessary for the initiation of a new chick must be included in the egg since the shell isolates the embryo from the environment until hatching. However, the hatching chick contains more cholesterol than does the original egg, indicating that the new tissues of the chick are synthesizing this necessary substance during incubation. It is apparent that this compound is essential for growth of tissue.

Cholesterol is here to stay; we should be spending more time

studying its importance instead of attempting to reduce its concentration. Although volumes have been written about it, its physiological functions are still poorly defined. Accumulation of more facts indicates that cholesterol is not deleterious.

Before our forefathers signed the Declaration of Independence, a French chemist crystallized a new compound from gallstones. The flat, flaky crystals looked like boric acid; they were insoluble in water, but they readily dissolved in the solvents for fats. Later work proved that they belonged to the wax family. In 1815 another Frenchman named the new compound "cholesterol," meaning "solid bile," from the Greek. In German it is called "cholesterine".

Cholesterol is widely distributed only in animal tissues. Most bacteria do not contain it, yet small quantities are found in the colon bacillus, a native of the colon in higher animals. Some of the protozoa will not grow without cholesterol; however, it must be furnished in the food since the lower animals cannot synthesize their own requirements. In the mammals each cell contains not only cholesterol but also the enzymes necessary for local production of the compound. Apparently the local need for it may be too sudden to depend upon dietary intake or mobilization from other tissues in the body.

For years it has been known that the liver could synthesize new cholesterol; this organ was considered the major source of endogenous production. This theory has been disproved by the recent work of Wilson (6). During the digestion of a fatty meal, the liberated fats are insoluble in water or blood serum. The cells of the intestinal tract synthesize cholesterol whose combination with the fats render a soluble union that can be transported through the blood to the storage depots or to the tissues burning the fats as fuel. It would be unhandy for the intestinal tract to send a message to the liver for a new supply of cholesterol to combine with the fats; the fats would be polluting the intestinal cells until the cholesterol arrived. How much more efficient for the intestinal cells to produce instantly the exact amount of cholesterol needed as the fats are absorbed.

Cholesterol can be synthesized from the simplest organic compounds. The starting molecule is only a two-carbon chain;

hence, it is available in carbohydrates, proteins, or fats. Regardless of what we eat, there is always an abundance of building material for this substance. Diets of animal origin furnish the individual with some exogenous cholesterol. On the other hand, the vegetarian must synthesize all of the compound needed by his tissues. Since vegetable fats are more soluble in water than are animal fats, less cholesterol will be synthesized in the intestinal mucosa during absorption of the vegetable fat; consequently, the cholesterol in the blood will be lower.

These observations place a new interpretation on some old facts. It is not the cholesterol in the diet which raises the serum cholesterol of the meat eaters, but it is the cholesterol synthesized in the intestinal wall for absorption of fats in the meat or eggs. If as much as 25 gm of pure cholesterol is added to the diet of a vegetarian, very little is absorbed; the majority is passed out through the feces. The significance of this observation will be discussed in more detail in a subsequent chapter on low cholesterol diets. It is apparent that another function of the compound is that of making insoluble fats available to the body.

In the mammal, the cholesterol content of the numerous tissues varies widely. The highest concentration is found in the adrenal glands; over 7 percent of the fresh weight is due to this substance. In the brain and spinal cord about 2 percent of the weight is due to it. The kidney, spleen, and liver follow in order with less than 0.5 percent each. The blood contains a smaller amount than the liver, while of the major organs the muscles have the least concentration. Very little cholesterol is found in the bones, but ten times this quantity is present in the marrow inside the bones. The bone marrow is continually forming new blood cells, and cholesterol is important in this process of growth.

At the time of birth, the human tissues contain about the same concentration of cholesterol as the corresponding tissues in the adult except for the brain, the adrenals, and the blood, in which smaller quantities are found. Without digestion of fats in the gut, the fetal blood has not been flooded with newly synthesized cholesterol. The adrenal is relatively inactive in the fetus and apparently does not have the demand for cholesterol as seen postpartum. The huge quantity of this compound in the brain is

added after birth during the development of the functions of this organ. During this growth period, the brain can synthesize its own cholesterol, but in the adult this potential is lost. The cholesterol in the adult brain is relatively stable and is seldom replaced; the enzymes necessary for synthesis disappear.

Although the adult brain and spinal cord make up only 2 percent of the total body weight, they contain 23 percent of the total cholesterol. Since there is very little wear and tear requiring replacement of this substance, it is considered to be a part of the supporting structure rather than to be concerned with metabolic activity of the central nervous system. Some feel that it may be insulation for the multitude of nerve fibers in order to avoid short-circuiting, similar to the use of rubber on electrical wires.

The body of a man weighing 150 pounds contains about one-third of a pound of cholesterol. The total amount in the muscles is about the same quantity as that in the brain, or 23 percent; this may be necessary for the fat content of muscle tissue. The connective tissues that support the various organs contain a similar quantity. Fats are needed as nutrition in the muscles and connective tissues; it is the cholesterol that makes the fats soluble. The skin contains about 10 percent of the total cholesterol; in this organ a definite function is known. Sunlight acts on the cholesterol in the skin producing Vitamin D which prevents the bent bones of ricketts. The skin bears the brunt of most wounds, and cholesterol is essential in the growth of replacement tissue.

The concentration of cholesterol in the blood varies widely. Most of it is bound to fats or proteins for the transfer of food to the storage depots or to the tissues for fuel. Apparently the higher concentration found in populations consuming meat and dairy products is due largely to that synthesized in the intestine.

During starvation, the body is sustained almost 100 percent on fat from the storage depots. On an average American diet, only 40 percent of the calories comes from animal fat. Either source releases cholesterol when the fat is burned. However, in starvation the stored fat is already combined with cholesterol making it soluble and immediately ready for use. Without the daily synthesis of this compound in the intestinal tract, the serum level falls as low as that seen in individuals eating a low cholesterol diet. The

average American living over 70 years of age shows no evidence of exhaustion of the intestinal cells which form the necessary cholesterol nor of the liver which disposes of it. No harmful effects from eating a high cholesterol diet have been demonstrated.

Excess or worn-out cholesterol is excreted by the liver. Most of it is converted into bile acids and bile salts which appear in the bile. These compounds are essential for digestion and absorption of foods in the intestinal tract. Some free cholesterol is present in bile; if needed, it may be re-cycled. Thus, another function of cholesterol is to furnish the bile salts.

With the exception of the brain and skeleton, the cholesterol in the tissues is changed frequently. This is demonstrated by using the Geiger counter to follow radioactive cholesterol through the tissues and its eventual excretion. The adrenals have the most rapid turnover. Although both glands sitting above the kidneys weigh only a fraction of one ounce, their concentration of cholesterol is the highest of any organ. During stress, 50 percent of the substance may disappear in a period of three hours, but the normal concentration is restored forty-eight hours after the stress is over. It was no accident that so much cholesterol is stored in the adrenals.

Cholesterol is the starting point for the manufacture of the adrenal cortical hormones so essential to life and emergencies. If the adrenals are removed, in a few days death follows due to low blood pressure, a lack of nutrition to the cells, and a lack of proper mineral levels in the blood. It is the function of the adrenals to maintain homeostasis, the constant levels of nourishment and a constant environment for the cells in the body. Without this regulation of the constituents in the blood, a minor illness would upset the balance, and death would ensue. Cholesterol is essential for the body to meet stress and to survive emergencies.

So far it has been shown that cholesterol is essential for the life of man from the sperm cells, through growth, for nutrition, and for the replacement of worn-out tissues. But that is not all. Reproduction of the human depends upon cholesterol. The latter compound is the starting point for the manufacture of the male

hormone which produces the broad shoulders, the beard, the deep voice, and the male genitalia.

The female sex hormone comes from the male hormone which goes back to cholesterol for its origin. Part of the feminine contour depends upon a lack of male hormone, and part of it is due to the female hormones themselves. The ovary produces two related hormones, one in the ovarian follicle and the other in the corpus luteum cells at the site of the ruptured follicle after the egg is extruded. Perhaps Adam did come first since the male hormone precedes the female counterpart, but it must have taken a tremendous amount of female hormone to make a woman out of a male rib.

This brief summary of a few of the functions of cholesterol clearly indicates that it is indispensable for many of the body's intricate physiological processes. What about evidence that it is deleterious? Only a solitary observation made years ago suggests that it might be harmful. The atheromatous plaques on the inside of the arteries are high in cholesterol. This compound is essential for building new tissues, as detailed above. Atheromas are new scar tissue repairing lesions on the surface of the blood vessel. Without such a plaque, an ulcer would penetrate the wall, and fatal hemorrhage would occur.

Did the cholesterol start the injury to the blood vessel in the first place? There is absolutely no evidence for such a thought. If this were true, one would find lesions in the delicate forming arteries in the fetus or in those in the incubating chick. Atheromas occur in blood vessels suffering greater stretch with each heart beat, near bifurcations where eddy currents are formed. Fair wear and tear are likely to initiate the disease, and cholesterol is mobilized to heal the wound. Here again, it is a friend and not the alleged foe.

No jury of sound mind would convict cholesterol of being a villain on the mass of evidence presented above. Case dismissed!

Chapter IV

THE CHOLESTEROL THEORY MUST GO

IT is apparent from Chapter 3 that cholesterol carries out important physiological functions, and cannot be executed and eliminated from our society. Furthermore, the accusing evidence is all circumstantial; a criminal cannot be hung on circumstantial evidence. Those who would condemn cholesterol have built an imaginary jail whose four corners are based on established facts. But, like all circumstantial evidence, the facts may have more than one interpretation. Additional new evidence has now exonerated cholesterol in the riddle of heart attacks.

Chronologically, the first cornerstone supporting the cholesterol theory was laid in 1913 when Anitschkow (7), a Russian scientist, discovered that after feeding rabbits huge doses of cholesterol, atherosclerosis appeared in their arteries. These atherosclerotic lesions contained cholesterol; naturally a cause and effect relationship seemed established. A more rational explanation for the rabbit experiment will be presented after the other three cornerstones are in place.

The second cornerstone came only three years after the first. In 1916 DeLangen (8), a Dutch doctor in Java, observed that among the natives the serum cholesterols were lower than those among inhabitants of Holland. Yet, if the Javanese obtained employment on the Dutch boats and ate the Dutch diets, their cholesterol levels soon approached those of the Dutch. The consumption of cholesterol was considerably higher in Holland than in Java. Furthermore, diseases accompanied by atherosclerosis were more frequent in Holland. Again, it seemed evident that cholesterol was responsible for the differences in the two populations.

These observations started a series of epidemiological studies in other countries. It was soon evident that populations subsisting largely on vegetables had lower levels of serum cholesterol and

fewer deaths from diseases with atherosclerosis. The nations using more animal products in their diets soon saw a rise in heart attacks with an acceleration as time passed. Unfortunately, attention had been focused on diet; other differences among the nations were neglected.

The third cornerstone was cemented firmly in place during World War II. By this time heart attacks were frequent in many of the European countries as well as in America. The war markedly reduced animal products in the diet; cholesterol intake fell. Heart attacks and other diseases with atherosclerosis promptly decreased in Europe, while no change in America was observed. Keys (9) stated that a change in diet was the only reasonable explanation for the reduction in Europe. Meat was rationed in America, but consumption was much higher than in Europe. Shortly after the war, heart attacks again rose in Europe as the nutrition improved.

This was the perfect experiment for the supporters of the cholesterol theory. Millions in Europe had had a reduction in cholesterol intake, and atherosclerotic diseases had fallen precipitously. When the former diets were resumed, the atherosclerotic diseases again rose. But a perfect experiment changes only one variable at a time. The understatement of the century would be that diet was the only thing that changed during the war!

The fourth cornerstone appeared during the Korean conflict. Enos (10) reported 300 autopsies on American soldiers killed in combat; in 77 percent there was atherosclerosis of the arteries to the heart. Although no measurements were made, he suspected considerable narrowing of the lumen. It is significant that none of the individuals had a record of any heart symptoms. Their ages ranged from 18 to 48 years; in 200 cases the average age was 22.1 years. Since the Koreans did not show a similar degree of atherosclerosis, the proponents of the cholesterol theory immediately pounced upon the report. Allegedly, diet was the only difference between the two groups; Congress and the military were urged to change the military diet. Fortunately, in a crowd there are always some cool heads. A different interpretation of the facts will be given later.

Needless to say, hundreds of experiments supporting the cholesterol theory have been reported, but if the four cornerstones

mentioned above were suddenly removed, the thesis would crumble like a wooden house attacked by termites. New evidence places a radically different interpretation on the four observations of facts. It is regrettable that some of our best scientists will be humiliated if the cholesterol theory is abandoned. However, medicine has no room for dogma; progress was delayed 1,000 years by Galen's theories which were not supported by adequate evidence.

More than fifty years of further observations leave no doubt that the first mistake was the use of rabbits by Anitschkow in 1913. If he had used rats, dogs or even man, he would have found that cholesterol-feeding would not have caused a marked rise in the serum cholesterol nor the development of atherosclerosis. Rabbits must have been on the "menu of the day" and were his only choice. Being a vegetarian, the rabbit never ingests cholesterol; his body is not equipped to dispose of the large quantities suddenly appearing in the experiment. A two-pound rabbit was given as much cholesterol as a 150-pound man normally eats.

Furthermore, all strains of rabbits do not react to cholesterol-feeding as did those employed by Anitschkow. Turner (11) studied this problem in 1938 and found that if those susceptible to cholesterol-feeding were given therapeutic doses of thyroid, the serum cholesterols were lowered, and the atherosclerosis did not develop. If he removed the thyroids from animals resistant to cholesterol-feeding, they promptly developed high levels of serum cholesterol, and atherosclerosis appeared. It became evident that a thyroid deficiency was far more important for the development of atherosclerosis in rabbits than was the presence of excess cholesterol. In a later chapter, overwhelming evidence will be presented that thyroid deficiency is a very potent factor in causing atherosclerosis in all species.

It seems fitting that the Russians, who started the cholesterol experiments in 1913, likewise in 1964 found that physiological changes other than cholesterol would explain the atherosclerosis. Malysheva (12) reported that before the atherosclerosis appeared in the cholesterol-fed rabbits, the metabolism of the animals fell to levels as low as that seen in rabbits with the thyroid removed. Later it will be pointed out that thyroidectomy alone, without

adding cholesterol in the diet, will produce atherosclerosis in herbivora. Thus, the initial cornerstone in the cholesterol theory has crumbled with time and with the additional weight of new evidence.

The appearance of atherosclerosis in some strains of rabbits was the only direct evidence that cholesterol might cause the disease. Now that a more rational explanation for the results is apparent, this alleged evidence becomes circumstantial and joins that from the underdeveloped countries and from World War II and the Korean conflict. In Chapter 3 it was pointed out that cholesterol is essential for growth of new tissue. Atherosclerosis involves the formation of scar tissue replacing damaged normal cells. It is reasonable to assume that the cholesterol in atherosclerotic lesions of rabbits is required for the new growth; there is no evidence that the cholesterol causes the pathology.

It was further pointed out in Chapter 3 that in the hen's egg and in the human fetus, delicate new blood vessels develop in an environment of cholesterol higher than that found in the blood of patients developing heart attacks. No atherosclerosis is seen in the chick nor the newborn baby. Many heart attacks occur in patients with serum cholesterols below the average normal. It is obvious that the cholesterol level of the blood is not the limiting factor in the development of atherosclerosis; a new theory compatible with more of the facts should be sought.

Cornerstones two, three, and four were not founded upon abnormal experiments on laboratory animals, but were concerned with observations on man himself. They would be of far greater significance if they supported the cholesterol theory. Recent autopsy evidence clearly shows that the results were not due to variations in the cholesterol in the diet. These three sources of circumstantial evidence must be adandoned. For clarity, each will be presented in a separate chapter. Cornerstone three will be considered next since its refutation places a new interpretation for cornerstone two.

Chapter V

THE AUTOPSIES SOLVE THE RIDDLE

IN Chapters 1 and 2 reference was made to autopsies at Graz, Austria. An explanation of their role in solving the riddle of heart attacks is in order. For 28 years most of my time had been spent on the problems of thyroid deficiencies in both animals and man. Personal observations confirmed long-standing reports in the literature that the thyroid was involved in atherosclerosis. It was felt that a goiter area in which the entire population suffers from thyroid deficiency would be an excellent site for the study of atherosclerosis occurring in routine autopsies.

Austria seemed to be a suitable place for such observations. The Alps have long been known to have goiter areas due to the absence of iodine in the soil and drinking water. Austria took the lead in medical education over two hundred years ago when the renowned Empress Maria Theresia passed a law that all deaths in hospitals must be autopsied. During the latter part of the last century, so many American doctors flocked to Vienna for postgraduate study that they formed their own American Medical Society of Vienna in 1879. It is still active today; through it my wife and I were introduced to Austria in 1958.

Vienna is on the plains and does not suffer from endemic goiter. In driving through the Alps searching for a suitable area, it was learned from the physicians at the small hospital in Eisenerz that Professor Ratzenhofer in Graz had done some work on the thyroid gland. Luck was never kinder to an itinerant scientist. Professor Max Ratzenhofer had never heard of me, nor I of him, but his keen interest in science and his graciousness in sharing his data established at once a cooperative program that has continued to date.

Graz is a charming city with a long and colorful history. It was founded over eight hundred years ago, and descendants of some of the early settlers are still there. A fortress constructed on top of a

mound of rock 300 feet high was one of the strongest bastions in Europe. For three hundred years it resisted repeated assaults of the Turks; even Napoleon could not conquer the town when he overran Europe. However, he gained access after the rest of the country surrendered. Because he was so miffed by the tiny Goliath, he blew up the fortifications with dynamite. They were never rebuilt; some of the exposed dungeons survive today and are incorporated into an outdoor theater for summertime drama.

This second largest city of Austria has a population of over 230,000 with one main hospital, Das Landeskrankenhaus, which serves all strata of society, the rich, the poor, the imbecile, and the university professor. The medical school, one of three in the country, is over one hundred years old, and has the largest Pathological Institute in the world. Professor Ratzenhofer is the director. All of the surgical specimens from a population of one and one-half million are funneled into this laboratory. About 75 percent of the total deaths in the city are autopsied here each year; there are over 2,000 post-mortem examinations annually. These accurate diagnoses reflect changing death patterns at once.

In our first conference with Professor Ratzenhofer he stated that the entire population developed atherosclerosis as age advanced. He was almost correct; among the first 10,000 protocols reviewed, only one old lady of 70 failed to show arterial damage. She must have been a tourist, but it cannot be proven. Annual vacations have permitted sufficient time to personally review over 70,000 consecutive protocols of the meticulously prepared autopsies covering the years from 1930 through 1970. This wealth of clinical material illuminated the rise in heart attacks and other changes in death patterns as clearly as Darwin's travels supported his theory of evolution.

The first preliminary report (13) covering the years 1954-1958 revealed that at 30 years of age, 9 percent of the deaths showed visible atherosclerosis. This rose rapidly, and by age 60 the affliction had risen to 72 percent. Above that age it was rare to find an individual without scarring to the arteries. It was gratifying to find far more damage to the arteries in Graz than is encountered in the United States; there was no question about the inhabitants of Graz being low in thyroid function. Iodized salt had

not been employed as yet; goiters were frequently seen on the street, or found at the autopsy table.

These observations supported the thesis that thyroid deficiency enhances atherosclerosis. But immediately a fly appeared in the ointment. The number of heart attacks in these patients with a greater prevalence of atherosclerosis was only about one-tenth that seen in the United States. This came as a shock; the incidence at Graz was about equal to that seen in the underdeveloped countries eating a low cholesterol diet. It would take more than a vivid imagination to make Graz an underprivileged society. Their diet was very similar to that in America. Dairy products were inexpensive, and the Austrian has long been known to enjoy his Schlag (whipped cream).

Graz has been an industrial city for years; in fact, the Iron Age was born only a few miles away where the Romans fought the Celts for the famous mountain of iron. Their University has won its share of Nobel prizes, so that in no sense can the area be called backward. Here was the first modernized society in which heart attacks had failed to rise. Here was the exception to the rule that with affluence comes heart attacks. But this exception did not prove the rule; it only destroyed it.

Attention was next turned to the World War II years and the third cornerstone in the cholesterol theory of heart attacks. The qualitative drop in heart attacks reported from all over Europe during the war could be quantitated in the accurate protocols at Graz. In 1939 at the start of the war, 12 heart attacks per 1,000 autopsies were recorded. In 1945 there were only 3; the drop amounted to 75 percent. The inhabitants of Graz were affected exactly as those in other European countries.

But another shock was hiding in the autopsies carried out during the war. It had been assumed without any proof that the low cholesterol diet during the war had arrested the development of atherosclerosis; hence, fewer heart attacks. At the post-mortem examinations, the aorta and the vessels going to the heart are routinely opened, and the appearance of the lining carefully recorded in the protocols. At the height of the war, the number of protocols showing atherosclerosis below the age of 50 years was approximately double the number seen before the war. Further-

more, the degree of damage to the arteries of each of these individuals was also doubled when scored on a scale from 0 to 4. In other words, atherosclerosis had increased fourfold in a short period of 5 years, yet heart attacks had fallen by 75 percent!

This was a paradox and cast serious doubt on the cholesterol theory. The answer was very simple. If patients were not dying with heart attacks, what other diseases were claiming their lives? Consequently, a review of all causes of deaths among individuals between the ages of 30 and 60 were tabulated. The most outstanding change was an explosion of tuberculosis. Other infectious deaths also rose but tuberculosis will illustrate the point. In 1939, tuberculosis was responsible for 27 deaths per 1,000 autopsies among men in this age group. In 1944, the same disease had killed 55 similar-aged males. Deaths from tuberculosis occur at a much younger age than do those from heart attacks.

Tuberculosis alone had eliminated 28 potential candidates for heart attacks before their arteries were fatally occluded. A rise in other infectious deaths had removed many more. The drop in heart attacks had been only 8 per 1,000 autopsies. There was no paradox. During the war, less cholesterol was ingested, but other factors had caused a marked increase in atherosclerosis. Tuberculosis and other infections were killing those with accelerating atherosclerosis before heart attacks could occur. The drop in the latter during the war was not due to less cholesterol in the diet, but was due to a deterioration in health with a consequent rise in infectious diseases.

These observations showed very clearly why Graz had never had a high incidence of heart attacks. Infectious diseases had always been more prevalent in this location than in other modernized areas. This was not due to inferior health regulations, but was related to one of Mother Nature's variations. The lack of iodine in the soil and water had rendered the inhabitants deficient in thyroid hormone for centuries. It will be pointed out in a later chapter that one of the outstanding symptoms of thyroid deficiency is an increased susceptibility to infectious diseases. Sanatoria care did not reduce tuberculosis in Graz as it did in many countries. A "new population," described in Chapter 1, could not rise in Graz.

The other countries in Europe seeing a drop in heart attacks during the war had a rise in deaths from tuberculosis comparable to that in Graz. There was no rise in tuberculosis in the United States; there was no decrease in heart attacks. England had a smaller rise in tuberculosis and a correspondingly smaller drop in heart attacks than was experienced by the occupied countries. Germany had a tremendous increase in tuberculosis and a reciprocal fall in the number of heart attacks. There seems little doubt that the drop in heart attacks during World War II was due to the elimination of potential candidates prematurely by tuberculosis and other infectious diseases.

Thus the third cornerstone in the cholesterol theory, which allegedly was made of indestructible granite, turned out to be just ordinary clay. It has crumbled, leaving no support for the cholesterol theory. It was true that less cholesterol was consumed during the war, but this did not prevent an increased atherosclerosis found at autopsy. It was circumstantial evidence that less cholesterol produced fewer heart attacks; it is factual evidence that a rise in infectious diseases was responsible for the decrease in heart attacks.

During the latter part of the last century, autopsy reports from Germany appeared describing complete closure of the arteries to the heart in cases of sudden death. About the turn of the century it was realized in Canada and in the United States that this condition was increasing in frequency. In 1912, Herrick (14) of Chicago correlated the symptoms of heart attacks with the autopsy findings, and described treatment that allowed some of the victims to survive.

Some radical changes had been taking place in the death patterns before the rise in heart attacks began. In 1870 the deaths from tuberculosis had been 270 per 100,000 population. England, Germany, France, and other European countries had even higher rates due to the crowding in the cities. At that time sanatoria care for tuberculosis began, and the death rate fell precipitously. By 1900, less than half the previous number of deaths from tuberculosis were occurring. A "new population" was appearing among whose members heart attacks were more numerous.

At Graz the high incidence of deaths from tuberculosis and

other infectious diseases continued unabated until the end of World War II. It was the use of antibiotics (15) that finally reduced the carnage from infections in that city. In 1945 only 3 heart attacks per 1,000 autopsies were recorded, but the following year they started to rise and have been accelerating ever since. In 1946 the diet was low in cholesterol, there was little smoking since cigarettes had not been available to the civilians during the war, there should have been less stress since the war was over and there was hope for the future, the automobile had not arrived, and everyone had plenty of exercise.

Many of the factors allegedly preventing heart attacks were present, yet this disease suddenly began to climb. Why? As pointed out above, the war had caused more atherosclerosis than was present before or even 15 years later. Tuberculosis deaths had fallen remarkably between 1944 and 1945. Although most deaths from tuberculosis occur among the young, there are always a few near the age of 60. In 1945 there were 39 deaths from tuberculosis over the age of 60. If tuberculosis did not cause deaths in this age group, heart attacks should claim some of them soon, and they did. At that time heart attacks occurred only in elderly patients at Graz. Of the few cases seen in 1930, the average age was 68 years. Of the 167 cases observed in 1970, the average age was 66 years. Heart attacks were not decimating the younger population; however, after 1960 a few early deaths from this disease began to appear.

A plausible explanation for a rise in heart attacks immediately after the war was the prolongation of lives of patients suffering from tuberculosis. Eventually all of this source will be exhausted. But other infectious diseases killing infants and children are also being reduced. Some of these survivors should develop heart attacks near 60 years of age. They should not appear in the statistics until the year 2005. A few individuals are more susceptible to atherosclerosis and develop heart disease at a much younger age. As mentioned previously, those with a history of pneumonia are more susceptible to heart attacks before the age of 40. If a youngster survived pneumonia in 1946, thanks to antibiotics, he might be eligible for a heart attack by 1966. There appeared in the autopsies that year one case at the age of 28. It is

not known if he had been susceptible to pneumonia, but he surely was unusually prone to atherosclerosis. Heart attacks at such an early age are unknown in any country with a high incidence of infectious diseases.

In most countries "the new population" of senior citizens susceptible to infectious diseases has been accumulating over the past one hundred years, but in Graz such individuals appeared only since the use of antibiotics twenty-five years ago. Since the average age of heart attacks is over 60 years, Graz should lag behind the other modernized countries in this disease for another thirty-five years. At least this interpretation readily accounts for the low incidence of heart attacks at the present time in this highly developed society.

Thus the autopsies have solved the riddle of heart attacks. There remains no mystery about this disease which has surpassed all others as the leading cause of death. To a large extent, natural consequences rather than changes in our environment have been responsible. As the infectious diseases have been reduced, the survivors have lived into an age group in which degenerative diseases claim their lives. Why this group of adults is unusually susceptible to only a few of the degenerative diseases, such as heart attacks, emphysema, and lung cancer, remains a mystery. The possibility exists that stress, pollution, and a host of other factors may play minor roles, but their influences are not as yet clearly demonstrated. The autopsy studies during World War II leave little doubt that a return of infectious diseases would eliminate at once our leading cause of death. The rise of heart attacks is a crown of glory to the progress in medicine.

The lessons learned from these autopsies make untenable the idea that diet was responsible for the drop in heart attacks during World War II. This was cornerstone number three in the cholesterol theory. Furthermore, the same autopsies force a new interpretation for the low incidence of heart attacks in the underprivileged countries, cornerstone number two. The latter will be discussed in the following chapter.

Chapter VI

DOES A LOW CHOLESTEROL DIET PREVENT ATHEROSCLEROSIS?

THE second cornerstone in the cholesterol theory was based on the scarcity of heart attacks in countries eating diets low in cholesterol. This evidence began in 1916 with DeLangen's (8) observations that the Javanese, eating largely a vegetable diet, had lower serum cholesterols and fewer diseases from atherosclerosis than the residents of Holland. One exception to the rule has appeared: the Samburo tribe (16) in northern Kenya subsists largely on the milk of their cattle and consumes more cholesterol than any other known society, yet the incidence of heart attacks is not high. Later in this chapter, the discrepancy will be explained.

In Chapter 3 it was pointed out that the lower cholesterol levels in populations eating less cholesterol were not due to the absence of this compound in the diet, but rather were due to the lack of animal fats which require the synthesis of large quantities of cholesterol in the intestine for absorption of the fat. Of course, if cholesterol were toxic, that which is synthesized in the intestine would be just as harmful as that in the diet. But the evidence now seems conclusive that diets low in cholesterol offer no protection against atherosclerosis. For years, scattered autopsy reports had indicated mild atherosclerosis in underdeveloped countries; these were ignored since heart attacks were rarely seen.

In 1969 Strong (17) reported over 4,000 autopsies on babies, children, and young adults from five underprivileged areas. These included the Charity Hospital at New Orleans, and hospitals in Santiago, Costa Rico, Guatemala, and Durban, South Africa, where the Bantu were examined. His results clearly show that, in spite of minimal cholesterol intakes, many children below the age of three and all of those over three have beginning atherosclerosis. These early lesions involved the aorta more often than the arteries to the heart, but the latter arteries were involved in 90 percent of

the cases by the age of 30. The severity of the lesions progressed with age.

These clear-cut results distinctly show that diets low in cholesterol do not prevent early atherosclerosis. In fact, quite the converse is true; autopsies on better-fed Americans or on those of any nationality eating a similar high cholesterol diet show far less atherosclerosis in children and young adults. In the underprivileged countries, obviously something happens between childhood and middle age that prevents early atherosclerosis from progressing to heart attacks. Before presenting a rational explanation for the facts, a few previous reports agreeing with Strong's results will be mentioned. There has never been sound evidence that diet affected heart attacks; the confusion has arisen from a lack of critical evaluation of published reports.

In 1945 Becker (18) reported 3,000 consecutive autopsies on the Bantu of South Africa covering the years 1924-1938. He found only 6 cases of heart attacks, which sounds like a very low incidence. It was his work that stimulated a tremendous amount of effort seeking the secret of the Bantu. A critical examination of his data at the time would have prevented a waste of scientific manpower and taxpayer's money.

In the first place, 25 percent of the deaths were due to tuberculosis. This is a higher incidence than that found in the United States one hundred years ago when no heart attacks were recognized or reported. It has been mentioned above that tuberculosis kills the young adults. This would materially reduce the age of the adult population, and Becker's data reflect this. Among the 3,000 autopsies, only 352 cases had reached the age of 50 years. Six heart attacks in a population of 352 potential candidates are quite different from 6 in 3,000 autopsies. It seems more plausible that it was elimination of patients susceptible to infectious diseases (other infections were as numerous as tuberculosis in the Bantu) that was responsible for the low incidence of heart attacks rather than a low cholesterol diet.

Fortunately the autopsies at Graz in 1930 were carried out about the same time as Becker's observations on the Bantu. Deaths from tuberculosis were also high at Graz where they were 17 percent compared with 25 percent in the Bantu. In Graz 13 heart

attacks were observed in 769 cases over 50 years of age. The incidence of heart attacks is identical in the two groups, yet the Bantu were on a low cholesterol diet and the Austrians on a relatively high intake. Scientists were misled by Becker's data because the statistics were not corrected for age. His records revealed more early atherosclerosis in young adults than that seen at Graz.

In 1954 Higginson (19) reported autopsies on 523 Bantu over the age of 20. His data was not diluted with children among whom no heart attacks would be expected. Only 4 heart attacks were encountered; on the surface this number seems rare. However, scrutiny of his data reveals some shortcomings. Tuberculosis again was the leading cause of death, accounting for over 12 percent of the total. Only 48 of the 523 in the series were over 50 years of age and can be considered potential candidates for heart attacks. Four out of 48 possibilities shows almost a fourfold increase in the number reported by Becker ten years earlier. Each of the 523 patients showed some early atherosclerosis. Something was happening to the Bantu; it was not a high cholesterol diet. The number of tuberculosis deaths had been cut in half in the autopsy series; undoubtedly this factor must be considered.

The World Health Organization reported a marked drop in tuberculosis among the colored South Africans during the 1950's. It comes as no surprise that the incidence of heart attacks is continuing to rise. In a 1960 report Laurie (20) insists that heart attacks are not a rare disease in the Bantu. In a period of six months 6 cases of proven heart attacks were admitted to a medical ward. One of the autopsied cases was only 22 years of age, two were 40, one 48, one 58 and one 65. It is apparent that the younger patients with heart attacks are appearing among the Bantu as deaths from infections are reduced. The Bantu's alleged immunity turns out to be nothing but a high incidence of infectious diseases.

Autopsy studies from Japan have been cited to prove again that a low cholesterol diet prevents heart attacks. In 1956 Kimura (21) reported 10,000 autopsies carried out at Kyushu over a period of 40 years. He estimated that heart attacks were one-tenth that seen in the United States. Unfortunately, the presentation of his data is

not as detailed as that on the Bantu, and the incidence of tuberculosis and the age groups are not available. It is probably of some significance that the World Health Organization states that at the time of his report the death rate from tuberculosis in Japan was 12 times that in the United States.

In the same paper Kimura presents a graph showing the incidence of atherosclerosis in the arteries of the hearts of the Japanese in over 1,000 cases that he personally examined. Damage appeared by the age of 5; by 30 years of age 50 percent of the hearts were involved, and by age 70 almost 100 percent were affected. Parrish (22) noted in the autopsies at Yale that 12 percent of those over 70 years of age were free from atherosclerosis.

It is obvious from the Japanese autopsies that a low cholesterol diet does not prevent atherosclerosis. Like the Bantu and other underprivileged countries, this arterial damage did not progress to heart attacks as long as infectious diseases were abundant. Recent reports from Japan have indicated that heart attacks are now rising rapidly. In a six-year study on a large group, Johnson (23) reported 335 new cases per 100,000 patient-years of observation. This is about the same incidence as that found in the Anti-Coronary Club in New York in which all of the factors of diet, exercise, smoking, etc., were controlled. It seems reasonable that when the rate of infectious deaths in Japan approaches that in America, heart attacks in the two countries may be very similar.

It is apparent from the autopsies in Charity Hospital in New Orleans, from Central America, from Japan, and from the Bantu of South Africa that a diet low in cholesterol not only fails to prevent, but is accompanied by an increased atherosclerosis of young people. It seems doubtful that the low intake of cholesterol is responsible for the increased damage to the arteries since the body can readily synthesize any additional quantities needed. However, the poor diet in the underprivileged areas contributes to a low resistance to infectious diseases which in turn remove young members from society before heart attacks can occur.

It is now possible to construct a rational explanation for most of the facts relative to diet and heart attacks. It is true that the countries ingesting little cholesterol have a low incidence of heart

disease. However, they have a high incidence of infectious diseases including tuberculosis which eliminates young adults. In the modernized countries a high level of cholesterol is eaten, but with progress comes better medical care and fewer infectious diseases. In the last chapter it was pointed out that Graz had a high cholesterol intake, but infectious diseases kept the rate of heart attacks low until the antibiotics reduced the latter. A rapid rise began at that time and is accelerating.

The gradual rise in heart attacks in the moderized countries during the twentieth century has accompanied the gradual reduction in deaths from infectious diseases. The biggest jump occurred with the introduction of antibiotics, just as was demonstrated at Graz. The Samburo tribe in northern Kenya has subsisted on a high cholesterol diet for years. Milk makes up most of the diet; the saturated fat intake is 65 percent of the total calories, one-third higher than that in America. No figures are available for their incidence of infectious diseases, but their life span is comparatively short in view of the average age of the senior citizens. The elderly are classified between the ages of 34 to 90, with an average age of this group at 47 years. Certainly the number over 50 are in the minority. There was no evidence of heart disease in 178 examined.

It is apparent that a careful appraisal of the evidence that a low cholesterol diet prevents atherosclerosis has no facts to support the theory. The second cornerstone of the theory must be discarded, including all of the epidemiological evidence. The wrong interpretation was made because autopsy studies were not done in the beginning. The only remaining fact associating a high cholesterol diet and heart attacks is the high incidence of atherosclerosis in the American soldiers killed during the Korean conflict. The next chapter gives a new interpretation of these facts.

Chapter VII

WAR AND ATHEROSCLEROSIS

FROM the beginning the enthusiasts for the cholesterol theory have eagerly adopted any evidence supporting the thesis without concern for other factors which might have been responsible for the results. It comes as no surprise that they seized upon Enos' (10) report in 1953 that the American soldiers killed in combat in Korea had alarming damage to the arteries of their hearts. At once agitation began on the military and on Congress to change the American soldiers' diet. They assumed without investigation that diet was the only factor producing the atherosclerosis.

If the activists had taken time to read a little history about war and atherosclerosis, they would have found Groedel's (24) article entitled, "Observations on the Circulatory System of Combatants during World War I." A table presents the autopsy findings on German soldiers killed in combat between 1914 and 1918. It was realized that atherosclerosis appeared in much younger individuals in war than during peace. Below 20 years of age, 36 percent of the German soldiers showed atherosclerosis; by age 30 this had reached 90 percent; and by 40, all of the men showed heart damage. It seems reasonable to assume that the German soldiers in World War I were not eating the plush American diet supposedly causing premature atherosclerosis in Korea.

Groedel further states that autopsies during the Franco-German War of 1871 revealed the same premature atherosclerosis noted in World War I. Thus, one hundred years ago, long before heart attacks were recognized, and before polyunsaturated fats were thrust upon the public, war was known to hasten atherosclerosis.

Enos' series of American soldiers in Korea indicated that 73 percent had some degree of atherosclerosis. Their average age was 22 years. The German soldiers in World War I showed 76 percent at age 25, a very comparable figure. It is obvious that not diet but something else about war is responsible for the accelerated

atherosclerosis observed in the American soldiers. It will be recalled that a fourfold increase in damage to the hearts of civilians during World War II was noted in the autopsies at Graz. The surviving civilians vividly remember that they were not eating a high cholesterol diet at that time. Some of the other factors which influence atherosclerosis will be mentioned in a later chapter.

In 1971 McNamara (25) reported 105 autopsies on American soldiers from the Vietnam battlefields. The average age was again 22 years, but the incidence of heart damage was only 45 percent compared to 73 percent in Korea. Furthermore, by using a superior technique for measuring any possible interference with blood flow, it was found that only one individual had any degree of narrowing of the lumen of the arteries; in other words, no heart attacks were imminent. Among American civilians, a few heart attacks do occur in this age group. Personal observations on a 22-year-old male whose autopsy showed massive occlusion of the coronary arteries leaves no doubt that premature heart attacks can occur even in the absence of military duty.

Thus, the fourth cornerstone of the cholesterol theory has been founded upon fallacy rather than fact. The proponents have been over-zealous to accept new evidence without critical examination of it. They started the theory on atherosclerosis in a few rabbits fed huge doses of cholesterol. When later it was shown that other species, including the human, would not show the rise in cholesterol or the atherosclerosis, no attempt was made to adjust this information with their thesis. The low incidence of heart attacks in countries eating a low cholesterol diet was attributed to less atherosclerosis without the benefit of autopsies indicating the amount of atherosclerosis present. Recent autopsy studies clearly show that atherosclerosis is worse in the underprivileged countries. The inconsistency does not seem to disturb the theorists.

World War II was accompanied by a marked drop in heart attacks in Europe. Without looking at the autopsies, Keys (9), one of the leading proponents of the cholesterol theory, stated that no rational explanation other than a change in diet was evident. Autopsy studies now reveal more atherosclerosis during the war than before or afterwards. Although these preliminary reports of

Barnes and Ratzenhofer have been published, the enthusiasts have ignored them. Finally the premature atherosclerosis in the American soldiers killed in Korea was found to be no greater than in soldiers in previous wars in which there were no high cholesterol diets. Thus, none of the circumstantial evidence can be used to support the cholesterol theory. In fact, there is no convincing evidence that cholesterol is concerned with heart attacks.

In spite of overwhelming evidence, the activists have recently requested one billion dollars from the government to prove the dietary theory. If the present monograph fails to change their minds, perhaps we should call for help from the last court of appeals, the "Nadar Raiders."

Chapter VIII

A NEW WORKING HYPOTHESIS

THEORIES are created to correlate and explain apparently unrelated facts. As more facts are accumulated, it is often necessary to modify or even abandon the thesis. This is true for the cholesterol theory of heart attacks. As pointed out in the previous chapters, an entirely new theory is indicated.

A working hypothesis is an embryonic theory to be tested with more research. Over twenty years ago it became evident that many facts did not fit into the cholesterol theory; hence, a new approach to the problem was undertaken. It was quite by accident that my interest in heart disease arose.

In 1930 an energetic graduate student arrived at the physiology department of the University of Chicago. Professor Anton J. Carlson, a legend in his field, assigned the neophyte the subject of the thyroid gland for his doctorate thesis. The lad's heart sank since during his undergraduate studies he had worked on the female sex hormone; for some reason, sex seems far more exciting to young students.

There was no show of emotion, and Professor Carlson never knew about the disappointment. This was during the economic depression, and any job offering a chance to continue graduate school was welcomed with open arms. The work proved more of a challenge than had been anticipated, and within five years a life-long study raising more questions than answers was proving fruitful.

Among other duties it was necessary to teach the course in endocrinology to medical students each quarter. Laboratory animals were used to demonstrate the various syndromes seen after removal of each of the glands of internal secretion, or conversely, after administration of too much hormone illustrating overproduction of the glands.

One of the most dramatic demonstrations was that of the cretin rabbits produced by removing the thyroid glands from the babies when they were only 3 weeks of age. Within two weeks after surgery, their fur became dry and did not remain in place. Another week, and their weights were lagging behind those of the controls. As time passed, every cell in their bodies was affected and, as a result of repeated infections, they died at less than half the normal life span. Thyroid administration to these animals brought fast relief from their multiple maladies; their miraculous return to health left a vivid memory still present forty years later.

Medical studies were completed in 1937. Then began a steady progression of patients, many of whom had ill-defined complaints not fitting the usual categories of disease. Repeatedly, patients were seen whose physical findings simulated those of the cretin rabbits. At that time, if no organic disease could be found, it was customary for most physicians to label such an individual a "hypochondriac". The tremendous progress in medicine has offered little to such patients, but a more sophisticated name for them has appeared; they are now sufferers from "psychosomatic complaints."

Two tragedies within six months of graduation have served as a constant restraint against assuming that any complaint is imaginary. Other physicians had failed to find any reason for the peculiar symptoms of a girl in her late teens. Personal efforts were likewise unproductive, but within a few months she died unexpectedly, leaving no doubt that serious undiagnosed pathology existed.

The second case was a young expectant mother with many complaints including headaches. Competent neurologists had ruled out brain disease, yet shortly after birth of her baby girl she died from a brain tumor confirmed at autopsy. These two clinical errors illustrate that one should never discredit the patient's history. A second effort, a third or a fourth may uncover unsuspected pathology and save a wasted life.

The lessons learned from the baby rabbits suggested that diverse symptoms might occur in thyroid deficiencies; hence, any undiagnosed case was carefully screened for evidence of hypothyroidism. Several years were spent trying to find a more accurate laboratory aid in segregating patients in whom thyroid therapy might be

beneficial. The details will be presented in a later chapter, but suffice it to say, those individuals with symptoms of thyroid insufficiency consistently ran subnormal temperatures.

When other medications failed to relieve the patients' complaints, thyroid therapy was instituted if their body temperatures were subnormal. It soon became evident that many cases of alleged hypochondriasis lost their symptoms and developed a more optimistic outlook on life. Such a patient was not suffering from imaginary ills, but had been leading a life of misery due to chronic fatigue and altered metabolism.

As this class of patients improved, they told their relatives, their friends, and even chance acquaintances. A tiny rivulet of these individuals slowly grew into a stream, since a rational explanation of their complaints at a cost of a few cents a day was more enticing than expensive psychiatric care without relief.

A large general practice during a period of thirteen years revealed a sizeable percentage of patients whose problems were solved by thyroid therapy. Suddenly, in 1950 a new problem was thrust upon a relatively serene practice; the first heart attack occurred. This developed in a friend who had not been a patient prior to that time.

In going over his history it was apparent that he had suffered for several years from symptoms of low thyroid function but had never sought medical advice for them. It was realized then that heart attacks had been conspicuous by their absence in my practice during a decade when they were rising rapidly in the rest of the country. Was this a coincidence or did it have significance?

By this time, other evidence indicated that the thyroid deficiencies might be related to heart attacks. In the latter condition the serum cholesterol was often elevated; the cretin rabbits had high cholesterols. Cholesterol was being suspected as a culprit in heart attacks, and clinical evidence clearly showed that the thyroid function was intimately concerned with the level of cholesterol in the blood.

The role of thyroid deficiencies in heart disease certainly needed to be investigated. The seriousness of the rapidly rising heart attack problem seemed to justify adding this study to the existing program. Accordingly, routine pretreatment examinations

were broadened to include a 2-meter chest x-ray for heart size, a cardiogram, and appropriate blood studies.

Many patients were under observation, and some had been on thyroid therapy for ten years. More were being added all of the time and both groups would be evaluated for any evidence of heart disease at one- or two-year intervals. Hundreds of patients would have to be followed for many years to determine if there were fewer heart attacks among those treated with thyroid. In a private practice a similar group of controls could not be maintained; hence, a much larger group would have to be treated to establish validity of the results.

A working hypothesis was adopted that any patient with a subnormal temperature whose complaints were not amenable to other medications should be given a therapeutic trial on thyroid therapy. It soon became apparent that many with previously alleged "imaginary ills" no longer complained, and their outlook on life improved. They had more energy, accomplished their routine work more efficiently, and became interested in hobbies and recreation.

The role of the thyroid in other aspects of physiology will be discussed in later publications. The present report is restricted to its influence on heart attacks.

Chapter IX

EATING PROVES THE PUDDING

THE pattern for the search for truth has changed remarkably with other refinements in our civilization. There was no urgency in Mendel's study of inherited characteristics. Darwin did not travel by jet to hasten his studies on evolution. Each had time to think when not collecting data. They were spared the pressures of the modern scientist.

"Publish or perish" is the dictum of our modern colleges. Research grants from private or governmental agencies are made to those who can compile a rapid bibliography irrespective, at times, of the quality of the work. Such was not the case in solving the riddle of heart attacks. Many years could be spent before the results were evaluated. No grantor had to be satisfied; no tax money was being expended. Medical service was being furnished to a large group of patients without extra expense, and every effort was being made to bring them the latest advances for their particular problems. Each was aware that extra effort was being made to prevent the occurrence of a heart attack.

Time was taken to discuss the many factors associated with heart disease. Confusion over cholesterol required prolonged discussions to point out that our ancestors ate animal products, and did not suffer from sudden collapse. Patients were encouraged to eat a well-balanced diet with meat and dairy products in abundance, as was advocated by our leading scientists a generation ago. A personal life-long habit of two eggs and bacon for breakfast gave encouragement to many patients.

Cigarettes were given up in 1920, not because the Surgeon General threatened cancer, but because a tight budget for education did not leave money for the weed. Ash trays in the office said "welcome" to the smokers. In twenty years, cigarettes were restricted in only two patients; in each case, allergy was the indication. The evidence that smoking contributes to heart disease

is more statistical than real.

Exercise is left to the discretion of the patient. If some pleasure is derived from sports or manual work, there is no objection. Yet those who deliberately exert themselves for health reasons are probably wasting their time. More diseases have been cured by bed-rest than by expending more energy. The number of heart attacks occurring among the joggers should dampen the enthusiasm for this type of unsupervised sport among the laymen.

Stress is difficult to control. How can one avoid the road hog in a traffic jam, or curtail a wife's spending habits at a time of unexpected "drought." Life was not designed to be a paradise; one must learn to roll with the punches. The autopsies during the war leave little doubt that stress aggravates atherosclerosis, and any unnecessary worry should be avoided. However, no psychotherapy was used to reduce the usual trials and tribulations in the series of patients observed during the present report.

Beginning in 1950, in addition to the usual screening for hypothyroidism, each adult was carefully questioned about a history of heart disease in the family, and each received a chest x-ray for heart size, a cardiogram, and appropriate blood chemistry. If any changes were made in diet, they included the addition of more saturated fats, including eggs and dairy products. No increase in exercise was recommended, and smoking was not discouraged. The only change in the daily routine was administration of a thyroid tablet to each individual having symptoms of thyroid deficiency, including a subnormal temperature.

It will be pointed out in a later chapter that no specific laboratory test is available for diagnosing hypothyroidism. For thirty years a very close correlation has been found between the symptoms of this disease and the temperature of the patient taken under basal conditions (26). Basal conditions signify that digestion is not going on, there are no effects of exercise, and there is a minimum of tension. All these factors tend to temporarily raise the temperature of the patient.

From a practical standpoint the best time to get the basal temperature is immediately upon awakening after a good night's sleep. Hence, the thermometer is shaken down well and placed on the bedside table before retiring. As soon as the patient awakens,

the thermometer is placed snugly in the armpit for ten minutes by the clock. In young children the rectal temperature is taken, since attempts to quiet them result in struggling which will elevate the temperature. Rectal temperatures of two minutes are adequate. Oral temperatures are often misleading since any respiratory infection, including sinusitis, will elevate the local temperature while the rest of the body may be subnormal.

The normal range is considered to be between 97.8 and 98.2 degrees Fahrenheit. Since the temperature of the female varies with the different phases of the menstrual cycle, comparable readings can be obtained on the second and third days of menstruation. It has been found that patients with symptoms of thyroid deficiency consistently run basal temperatures below 97.8 unless there is some intercurrent infection. Conversely, patients with overdosage of thyroid or those with a spontaneous excess of thyroid hormone run temperatures above the normal range. Any infection or even cancer will sometimes elevate the basal body temperature.

It is apparent that basal temperature is not a specific test for thyroid function, but it is a very useful tool in diagnosing and treating cases of hypothyroidism. Frequently, subnormal basal temperatures will be found in patients who are apparently in excellent health. They do not require treatment at that time, but subsequently they often develop symptoms which usually respond to therapy when needed. Furthermore, if too much hormone is administered, the basal temperature is quickly elevated above the normal range.

A high proportion of the patients were deficient in thyroid secretion since this phase of medicine had been my primary concern for many years, and hypothyroid patients gravitated to my office. To have denied any of these patients appropriate therapy would have constituted malpractice.

Fortunately, in 1957 there began to appear from a study (27) in Framingham, Massachusetts, reports which could serve as controls for the thyroid-treated patients. The Public Health Service supported a huge program to determine the occurrence of heart attacks in a typical American town. Over 5,000 adults were examined at two-year intervals in much the same manner as

patients in the present study. Those at Framingham did not receive thyroid; hence, they served to indicate the natural occurrence of heart attacks. With the proximity of Framingham to Boston, where so much emphasis has been placed on dietary alterations, exercise, and smoking, it seems reasonable to expect that many in that group may have been influenced by the propaganda of the time. If this were true, differences between those in Framingham and those receiving thyroid would be even more significant.

The Framingham study reemphasized many previously established facts about various factors in heart attacks. The disease is more frequent in males; a family history of the disease increases the risk; a high cholesterol level in the blood and/or hypertension are predisposing, and age increases the frequency.

Twenty years have elapsed since the present observations were begun. By grouping patients into the various categories used by the Framingham study, a direct comparison can be made between the incidence of new heart disease in the thyroid-treated patients and that observed as a natural consequence in Framingham.

TABLE I

SHOWING THE RARITY OF NEW CASES OF CORONARY DISEASE IN THYROID-TREATED PATIENTS

Sex	*Condition*	*Number Cases Treated*	*Patient-Years*	*Coronary Disease Expected***	*Coronary Disease Observed*
F	Age 30-59	490	2705	7.6	0
F	High-Risk*	172	1086	7.3	0
F	Age over 60	182	955	7.8	0
M	Age 30-59	382	2192	12.8	1
M	High-Risk*	186	1070	18.5	2
M	Age over 60	157	816	18.0	1
Totals		1569	8824	72.0	4

*Hypertension and/or Hypercholesterolemia

** Compared with the Framingham Study

The results in Table I show a consistent rarity of new heart disease in each of the categories. A total of 1,569 patients were in the study. Some had been on therapy for thirty years and none had been observed for less than two years, the minimum time to qualify for comparison with the Framingham group. It is apparent that both sexes benefited from the thyroid therapy, and that the high-risk patients as well as older individuals were likewise relatively immune.

There were no new cases of heart attacks below the age of 50; the youngest of the four was 56 and the oldest 61. Only four cases observed is 94 percent protection out of the 72 cases which might have been expected. In retrospect, several factors must be considered in the four failures. The single case without hypercholesterolemia or hypertension died at age 56; his father died with a heart attack at the age of 54. The patient was over 50 years of age before thyroid therapy was started. It seems reasonable to assume that advanced atherosclerosis had been present before therapy was begun.

In each of the four failures, the dosage of thyroid was only two grains daily. Basal temperature studies were not routinely carried out on them, and the possibility exists that the dosage was inadequate. In high-risk patients it seems desirable to check basal temperatures at least every four months and adjust the dosage of thyroid accordingly. No harm will be done as long as the basal temperature is not elevated above the normal range; atherosclerosis may be arrested if the temperature is kept within normal limits.

Only four new cases of heart disease among hundreds of patients treated for many years strongly suggests that the thyroid therapy was definitely efficacious. Similar results might be expected among patients relatively resistant to coronary disease. However, it must be borne in mind that the present study was carried out on thyroid-deficient patients. In a later chapter it will be shown that such patients are unusually susceptible rather than relatively resistant to atherosclerosis.

Furthermore, some of the patients in the present study dropped out for various reasons. Some moved to other locations, and their new physicians declined to continue the treatment. Some became

patients of other physicians who discontinued the thyroid because one of the thyroid function tests was normal. Still others refused to continue thyroid therapy after their symptoms of thyroid deficiency disappeared.

At least 30 fatal heart attacks are known to have occurred prematurely among those who discontinued therapy. A high percentage of young individuals in this group indicates an increased susceptibility to hardening of the arteries. Two were under the age of 30, one between 30 and 40, two between 40 and 50, and eight between 50 and 60. These were all premature heart attacks; in each instance, the individual had been diagnosed thyroid-deficient several years earlier at which time there was no evidence of heart disease. Thus, 13 out of the 30 dropouts had heart attacks before the age of 60; this incidence is approximately double that seen in the population as a whole. It would appear that the hypothyroid patient is more susceptible than others to the ravages of premature heart disease.

The youngest of the deaths among the dropouts deserves mention. He was first seen with a thyroid deficiency at the age of 17 and became free of symptoms on thyroid medication. He then went away to college and discontinued therapy since he felt that his problem had been solved. Without warning, he suddenly collapsed with a proven coronary occlusion at the age of 23, a month after graduating from college. Belatedly, his mother confessed that heart attacks were frequent in her family, but she had shielded the information from her son so he would not worry. Knowledge of his increased susceptibility might have prompted him to continue therapy; a tragedy might thus have been averted.

The results of thyroid prophylaxis of heart attacks indicate the importance of the patient's understanding all of the symptoms of thyroid deficiency. If the latter are clearly presented to the physician, he has an indication to institute therapy which appears so efficacious in preventing premature tragedies. The next chapter presents some of the bizarre symptoms seen in thyroid deficiency.

Chapter X

BECOMING ACQUAINTED WITH YOUR THYROID

SINCE there are no specific tests for thyroid function, it is obvious that diagnosis depends upon the symptoms and an "accurate guess." Some well-read patients may guess as accurately as some physicians. This was illustrated recently when a stranger requested an appointment for his wife who had been diagnosed psychosomatic by a competent physician and by a psychiatrist. When brought into the office on a warm day, she was shivering even though wrapped in a blanket. Obviously, her temperature was well below normal, and the rest of the bizarre picture fitted hypothyroidism. In two months on thyroid therapy, she was a happy, useful member of society rather than a resident in a sanatorium.

To insure normal thyroid function in the newborn, one must be sure that the mother's thyroid is furnishing adequate hormone during gestation. Miscarriages, toxemias of pregnancy with edema and elevated blood pressures, the births of dead babies at term, or deaths of babies shortly after birth, are indications for a careful search for other symptoms of hypothyroidism in the mothers. During twenty years of obstetrical work, the single case of toxemia was encountered in a patient who presented herself too late for relief of her symptoms of thyroid deficiency.

The importance of the thyroid hormone to the newborn was clearly demonstrated in dogs by Smith (28) and his co-workers at the University of Chicago. Administration of radioactive iodine to the expectant mother ten days before delivery destroyed the thyroid function in both the mother and the fetuses. Four of the nine pups died in the first week, four more by 5 weeks, and the sole survivor was a total idiot. He did not have the normal instinct to nurse and had to be fed by hand. If placed on his back, he would make no effort to turn over and would remain in that

position for hours. He never barked, never played, and died at 9 months of age from an intestinal obstruction after having eaten sawdust.

This profound lack of physical and mental development was clearly documented in babies before the turn of the century. Probably not more than 20 cases of congenital absence of the thyroid have been reported in the literature; it has been my dubious privilege to have seen only one in over forty years of thyroid work. Growth either ceases or is markedly retarded from the time of birth. There is a total lack of development both physically and mentally. The muscles never develop any strength, and the child never walks, talks, or seems conscious of the surroundings. Fortunately, death occurs at an early age due to repeated infections.

All variations from the extreme condition described above to the normal will be encountered in routine births. It is difficult to detect minor deficiencies in babies, yet this is the most crucial period for treatment. The development of the central nervous system after birth is very rapid, and unless thyroid deficiencies are relieved before 6 months of age, the mental processes will be irreparably damaged. At this age one is limited to the symptoms and physical appearance of the babies.

In the newborn the hypothyroid baby may be more quiet than the others and may sleep more. Its activity is definitely reduced. The face is likely to be broader than normal; it rarely changes expressions. The tongue may appear too large for the mouth due to the accumulation of fluid and mucin-containing protein in the tissues of the oral cavity. Respiration may be noisy from the edema of the respiratory passages. The baby may breathe entirely through its mouth for lack of space in the nose, and may appear to have a cold all of the time.

Personal experience includes only one such newborn who required thyroid therapy at the age of 3 weeks. The mother, the father, and the grandparents were all deficient in thyroid secretion which fact illustrates the family occurrence of this disorder. Within two months, respiratory difficulties of the infant disappeared and a normal child developed. Two sisters in another family required treatment as early as 2 months and 6 months,

respectively. The mother had been on thyroid for years, and some of her earlier children had required therapy. Hence, she insisted that her family doctor seek consultation for the new baby who was slow in development. Brain damage was narrowly averted. With her next baby, the family doctor sought consultation at once. This one also required thyroid therapy. In the absence of infection, the basal temperature is always low; this is the only test necessary for a diagnosis.

In the preschool child the history and the basal temperature must make the diagnosis. Most of these children with low thyroid function will have a dull, apathetic appearance and be less active than normal youngsters; yet, here a paradox appears. A few will be very nervous, hyperactive and unusually aggressive; emotional problems are frequent. They may cry for no apparent reason and object strenuously to any restrictions. Temper tantrums are common, probably related to undue fatigue. Such youngsters may sleep longer than others and be slow-starters in the morning. Their attention-span is short; they flit from one activity to another, without becoming engrossed in anything. They adjust poorly to family routines. Frequent infections anywhere in the body are almost pathognomonic of hypothyroidism.

Starting to school creates crises in the lives of many thyroid-deficient children. Their endowment of energy is so low that they lack self-confidence. They have been tied to mother's apron strings all of their lives, and they need her protection. Mothers compromise by going to school with them until they learn that other youngsters are playmates. They cannot sit quietly and study for their minds are wandering all of the time. They cannot concentrate; hence, their progress is slow. Since their lessons do not intrigue them, they disturb the rest of the class for attention. These children are miserable due to an unrecognized physical ailment.

Close association with other children increases the opportunity for respiratory infections. Removal of tonsils cures tonsillitis, but does nothing to correct low resistance to other types of sore throats, earaches and other complications. They become "problem children," and are sent to the psychiatrist who tries vainly to find some mistake in their environment. The most frequent error can

be traced to "whom their grandmother married," producing another generation of thyroid-deficient children. No child should be called lazy nor referred for psychiatric care until the basal temperature has been determined. Correcting subnormal temperatures will restore most children to normal performance.

Puberty brings more problems. The tired boys aggravate their fatigue by part-time jobs, thus further robbing their low-energy endowment. Sports take both time and energy away from their studies. Failures mount, and dropouts begin; some of these can be avoided with more critical physical examinations. The girls begin the menstrual cycles with periodical loss of blood which must be replaced. Low-grade anemia further depresses their energy levels. The formation of blood in the bone marrow is intimately connected with the temperature of the marrow. Those individuals with low temperatures have deficient rates of blood formation and are the ones who develop anemia. For twenty years, correcting low temperatures in either sex with thyroid therapy has eliminated the need for periodic iron medication. There is sufficient iron in our diet, but if the bone marrow is lazy, the iron is not utilized.

Many cases of menstrual irregularities are hypothyroid in origin. This was firmly established in the last century when thyroid deficiencies were first recognized. Many years of successful therapy led some of the leading gynecologists to state forty years ago that thyroid had cured more menstrual disorders than all other medications combined. Personal experience during the past forty years has confirmed these observations; about 90 percent of the patients responded to treatment, as reported a few years ago (29).

Unfortunately some of the more recent graduates in medicine have been brainwashed about the value of thyroid function tests, which are unreliable. Unless the tests confirm the diagnosis, patients are either denied thyroid therapy or have the medication discontinued if some other doctor previously prescribed it. Symptoms may have been relieved by thyroid; they may recur if the medication is stopped and disappear again if the therapy is resumed. Yet some physicians are adamant unless the laboratory test is positive.

Patients do not seek help to satisfy pseudoscience, but want relief from their ailments. Recently three hysterectomized women

were seen who had been operated on for excessive bleeding before the age of 25. None had been suspected of hypothyroidism, yet in each case numerous other symptoms of this disorder promptly disappeared upon adequate therapy. The odds are very high that needless surgery might have been avoided, and the privilege of raising a family would not have been denied had the surgeon sought adequate consultation.

At any rate, no mistakes will be made if basal temperatures are taken routinely in all cases of menstrual irregularities and if those individuals registering low are properly treated with small doses of thyroid. This includes the girls who have not started by age 14, those who start but are irregular, those who flow too heavily with clots which cause pain from distention of the cervix, those who are relatively sterile and have difficulty becoming pregnant, and those who tend to miscarry. All of such cases are not due to thyroid deficiency, but no harm will result from thyroid therapy for a few months to those who have low temperatures. Time is still left for a more critical study of the few failures, and much expense will have been avoided.

The symptoms of thyroid deficiency in the adult were clearly described by Ord (30) in 1878. The meticulous autopsy on his patient demonstrated that every tissue in the body was affected from the hair on the head to the toenails; cells were lacking in circulation and "garbage" was piling up, destroying normal function. It is no surprise that many of these patients have been classed as hypochondriacs since every part of their bodies seemed to malfunction. The more one studies the multiple ramifications of the symptoms of hypothyroidism, the more tolerance one has for the diverse complaints.

With the exception of a subnormal temperature, fatigue is probably the most common abnormal finding. Some patients state that they were born tired and have never been rested; this statement is literally true. Others will sink into their chairs in the examining room, sigh, and say that they are tired of being tired. As children, they were called lazy; as adults they are unable to efficiently accomplish their daily tasks. A recent national symposium on "The Tired Young Housewife" was devoted entirely to the boredom and lack of motivation of the individual. For years,

these same girls have been found to be hypothyroids. With proper medication they have regained the energy necessary for their jobs, and have changed their attitudes; in some cases, the husbands' carburetors have had to be adjusted to keep up with them. Their problems are physical and not psychological.

About 10 percent of the calls to the doctor's office are for headaches. Fatigue is the outstanding cause in most of these individuals. With a lack of circulation, the tissues retain fluids and swell. With careful quizzing, a case of migraine will reveal that the wedding ring cannot be removed from the finger during a siege, and shoes are too tight. The shoelaces can be loosened, but the skull cannot be unbuttoned to give the brain more room. A day or two of bed-rest stops the vomiting, allows the water to be excreted, and the patient is ready for more exertion. Some years ago, 100 cases who were receiving thyroid therapy were reviewed, and 95 of them had recurrences of their headaches only when periods of unusual stress were forced upon them. With better circulation their tolerance to fatigue had been raised. A few headaches are due to allergy, but the majority should be treated with thyroid before undergoing the allergy tests.

The circulatory system suffers severely from thyroid deficiency. The blood pressures are usually low in younger patients, although beyond middle age markedly elevated pressures are common. The rise may be due to hardening of the arteries to the kidneys, restricting their circulation. In experimental animals, fatal hypertension can be produced by reducing the blood flow through the kidneys with a metal clamp on their arteries. The pulse rate in hypothyroidism is usually slow, although in some cases where the blood pressure is very low the heart may speed up in order to furnish more blood to the tissues.

The heart beat is feeble in the thyroid-deficient, and the amount of blood ejected with each beat is reduced. Fluid accumulates in the tissues; the baggy eyelids in the morning may be an early signal. In advanced cases, fluid accumulates in the abdomen, the chest, and even in the sac around the heart. This condition can be produced readily in the sheep by thyroidectomy. As a result of the poor circulation, the hands and feet may be cold even in summer; more clothing is worn, and room temperatures

above normal are desired.

The skin may show eczema in babies, and pimples during puberty, which condition may persist into late adult life in some individuals. One baby with eczema comes vividly to mind even after more than twenty years. Rodney was 7 months of age when first seen. He had bleeding eczema of the skin all over his body. Since birth he had been kept in a strait jacket to prevent his scratching a fatal hemorrhage. Hospitalizations and dermatological consultations had been to no avail. Five months of thyroid therapy alone cleared his skin; his hands could be released for the joy of unrestricted movement so essential for all babies.

One case of adolescent acne had persisted until the age of 61 when this man was first seen with a heart attack. Following recovery he was put on thyroid to prevent further arterial damage; his acne soon cleared up. Boils at any age are often a common finding in hypothyroidism; in fact, during the last thirty years no case of boils has been observed that did not need thyroid, and none has failed to respond. The poor circulation of the skin renders it highly susceptible to any type of infection.

The skin may become dry, scaly, and in extreme cases resemble fish scales, hence the term, "ichthyosis." The nails may be brittle and grow very slowly. In either sex the hair may become dry, brittle, and fall out leaving bald spots. The hereditary, premature baldness in some males is not necessarily due to an under-function of the thyroid. However, these individuals may need thyroid therapy for other reasons. A lack of perspiration from the skin is an outstanding feature in thyroid deficiencies although the palms and soles of the feet may sweat profusely due to nervous tension.

The nervous system suffers just as frequently as does any other tissue in the body. Practically all of the 100 cases of myxedema reported by the British Commission had some form of mental trouble. All were slow in thought and response; memory was poor, and almost half of them had delusions, hallucinations, or frank insanity. A lack of muscular coordination and weakness led to frequent falling. The special senses such as sight, smell, hearing and touch were often diminished. Nervousness, irritability, and a requirement for an abnormal amount of sleep were common.

A lack of appetite does not preclude obesity, since these

individuals burn up less fuel than normal. Indigestion may be due to a lack of acid in the stomach; yet in cases under nervous tension, too much acid may be secreted and peptic ulcers may be present. Constipation may be extreme and often is an early sign in young children. Gallstones are more common than in normal individuals, since the stones are often made of cholesterol, and this compound is elevated in the blood of hypothyroid patients.

The high cholesterol is due in part to a reduced excretion of cholesterol by-products into the bile by the liver. Thyroidectomy in herbivorous animals results in an elevated serum cholesterol even though no cholesterol is consumed. Another outstanding blood change is the anemia, mentioned previously.

Urinary symptoms include copious excretion, since very little fluid is lost through the skin. However, fluid intake is reduced for some unknown reason in hypothyroidism. The retention of protein and fluid in the tissues may dampen thirst. The lack of sweating in children often aggravates the bed-wetting problem. The bladder cannot hold the overnight supply, and the undue fatigue prevents the normal stimulus from awakening the child. The bladder mechanism is intact since such children never wet their breeches during the day. Thyroid therapy is one of the most effective weapons in this condition.

Even the skeletal system does not escape a lack of thyroid hormone. In children a marked deficiency will result in stunted growth, but a paradox exists in minor deficiencies. During puberty, if the thyroid function is on the low side of normal, the individual may become unusually tall. Growth ceases when the long bones close the growing centers at each end of the bone. The stimulus to close these centers is a normal function of the thyroid hormone. If the latter is deficient, growth may continue for some time, and a new basketball player may result. During the past twenty years, it has been found that in either sex, individuals over 6 feet in height consistently run temperatures a little below the normal range.

Another characteristic of the thyroid-deficient patient is the increased susceptibility to infectious diseases. It was mentioned previously that the newborn baby without any thyroid function dies at a very early age; pneumonia is the most frequent cause of

death. Any location in the body may be attacked by micro-organisms at any age if the resistance of the host is decreased for any reason. This has been demonstrated in all species of animals investigated. Thyroidectomy in swine may lead to skin infections, arthritis, or even rheumatic fever with inflammation of the lining of the heart.

The increased susceptibility to infections in hypothroidism seems as marked for viral agents as for bacteria. The common cold or influenza are examples of viral infections. One infection after another is "the story of my life" in the thyroid-deficient patient. The youngster with repeated colds followed by complications such as tonsillitis, sinus infections, draining ears, mastoid infections, rheumatic fever, etc., may be treated with antibiotics, and his life spared, but until he is put on thyroid therapy he will develop another infection in a short time. Prolonged antibiotic therapy can be discontinued about two months after the proper thyroid dosage is established. Elderly patients do not require vaccines against the flu if their thyroid function is normal.

Dave's case will illustrate the effect of raising the patient's resistance. He was 79 years old at his first visit. His left ear had been draining pus since early childhood; he recalled that at age 7 it stopped for a time. For 20 years he had an osteomyelitis, draining pus continually from his left femur about halfway between the hip and knee. His temperature was 3 degrees below normal. He was started on thyroid therapy which not only improved his energy level but also cleared up the infection in his leg after 3 months, and his ear after one year. Eight years later he carelessly neglected the thyroid medication, and the ear again became infected. Therapy was resumed; drainage from the ear stopped, and the osteomyelitis never recurred. His heart finally wore out, and he died at the age of 89.

This long list of symptoms and physical findings falls far short of covering all of the details of complications in thyroid deficiency, but it illustrates the extensive and diverse nature of the disease. The public should become aware of these symptoms. Any person having one or more similar complaints is entitled to check the basal temperature before consulting the physician. My new patients save one office call when they have their temperatures to

substantiate their symptoms and physical findings. Thyroid therapy is not a cure-all for man's ailments, but the fringe benefits from the elimination of this unnecessary complication may make the difference between success and failure in serious disease or delicate operations. My wife was assisted in arresting a complicated case of tuberculosis over thirty years ago, before the arrival of the miracle drugs. Her last thirty years have been far more healthful than the first thirty because some of the annoying symptoms of hypothyroidism have been removed. No specialist can afford to deny his patient any help that he can give. Only the cost of a thermometer and a willing ear prevent elimination of thyroid deficiency from his practice.

Chapter XI

MEASURING THE ACTIVITY OF YOUR THYROID

IF heart attacks occur because the individual's thyroid gland is not producing enough hormone, and if administration of such hormone will prevent the disease, why not test the entire population for thyroid function and treat those found deficient? Unfortunately, even after one hundred years of intensive search, no specific test for thyroid function has appeared. Diabetes can be detected by sugar in the urine or by an elevated blood sugar, gout can be discovered by an elevation of uric acid in the blood, and kidney failure is accompanied by albumin in the urine and elevation of nitrogenous compounds in the blood.

The precise function of the thyroid gland is still unknown. Apparently it is a catalyst governing the rate at which each cell in the body converts foodstuffs into energy for life. When this transformation of raw materials into the specific compounds needed for life ceases, death occurs. To sustain life, specific compounds must be burned to produce heat, just as wood burns in the fireplace to warm the house. All such conversions of energy consume oxygen; for years the measurement of this compound was the only test for the activity of the thyroid gland.

The method was called the basal metabolic rate, or BMR. Basal refers to the minimum oxygen consumed when the body is only sustaining itself and not producing energy for anything else. Exercise, the digestion of food, tension in the muscles, or even worry will increase the rate at which the cells of the body use oxygen, producing more energy. Hence, under ideal conditions the BMR should be run at the end of a good night's rest; the last meal should have been digested and the food stored in the tissues; the patient should be lying comfortably in bed and the mind should not be disturbed by the tax burden or the blonde next door. These ideal conditions are "hard to come by."

The technical details of the test are anything but relaxing. A tight clothespin on the nose and a large rubber breathing tube stuffed in the mouth do not lull the patient to sleep. Some machines use a tight mask over both the nose and mouth, which may be more comfortable, but a patient with claustrophobia will tear the mask from his face in terror. In spite of numerous objections to the BMR, the results with it are as reliable as the barrage of sophisticated chemical tests that are confusing the modern physician.

These tests are too complicated to be understood by the layman or the average physician, but a discussion of the underlying principles and errors will put their significance into proper perspective. They are all based either on the amount of hormone stored in the thyroid gland or the amount carried by the bloodstream. Attempting to measure the amount of hormone being used up on the inside of the cells by either process is about as accurate as trying to measure a thrifty Scotchman's spending habits from the size of his bank account or the money in his wallet. The patch upon patch of his trousers gives a more accurate index of his frugality; symptoms of thyroid deficiency give a more accurate index of the effective thyroid hormone at the cellular level.

Before the turn of the century it had been established that the thyroid hormone was a large protein molecule and was stored in the thyroid gland as such. Today it is known that the hormone circulates in the bloodstream as a large protein molecule; if not the same protein as present in the thyroid, certainly in combination with other proteins. Furthermore, the active principle always contains iodine, the same preparation used in sterilizing wounds. It comes as no surprise that the first chemical test for thyroid function was a measure of the protein-bound iodine circulating in the blood, or the PBI. Unfortunately, the iodized salt ingested daily can combine with other proteins which do not have physiological activity. Nevertheless, for thirty years some otherwise competent clinicians swore by the PBI as an accurate index of thyroid function, while the rest of us swore at it.

Some years later the thyroid protein was chemically broken up and a simple iodine-containing amino acid with physiological

activity was isolated, synthesized, and found effective in hypothyroidism. This compound was called thyroxine (31), or abbreviated to T4 since it contained 4 atoms of iodine. At once some authorities accepted this new compound as *the* hormone representing the whole gland and insisted on using only it for replacement therapy. Unfortunately the PBI test would not detect this compound so a new test had to be devised. This was called the T4 test, which is specific for thyroxine.

Still later another simple iodine-containing compound was isolated from the thyroid protein; lo and behold it was 4 times more active physiologically than thyroxine. Since it contained only three-quarters as much iodine as thyroxine, it was called triiodothyronine (32) or abbreviated to T3. Undoubtedly those who had claimed thyroxine was the only active principle in the thyroid had red faces, but their apologies have not appeared. A new compound required a new test and immediately the T3 test appeared. The only complication is that the T3 test will not detect T4; the T4 test will not detect T3, and the PBI will detect neither, nor vice versa.

Only one other of the multiple thyroid functions tests will be mentioned. Attempts have been made to guess at the cellular activity of thyroid hormone by measuring the amount of radioactive iodine retained by the thyroid gland after drinking a small cocktail of the material. The amount of useful information gained does not justify the two trips of the patient to the radiation laboratory, to say nothing of the exorbitant cost. The results are like the bank account; they tell us nothing about how much is being spent.

Personal attempts to find a more satisfactory index of thyroid function continued for over fifteen years. Thirty years ago one of the oldest symptoms of thyroid deficiency seemed worthy of trial. In the absence of intercurrent infection, hypothyroidism is accompanied by a subnormal temperature (26). It is evident that the more foodstuffs that are burned, the more heat will be produced. The thermostat of the thyroid-deficient patient may call for more heat, but the body is incapable of maintaining a normal temperature. On the other hand, if too much thyroid hormone is circulating, so much heat is produced that the

thermostat cannot control it; a low-grade fever results.

Some of my colleagues will remind you at once that there are other diseases that will produce a low or a high temperature. This is readily admitted, but the same diseases will affect the basal metabolism in the same manner. It is not claimed that the basal temperature is specific, but it is more accurate than the old basal metabolism and costs nothing. More information can be brought to the physician with only a thermometer than can be obtained with all of the thyroid function tests combined. After more than forty years of effort in this field, occasionally only the thermometer avoids a mistake in diagnosis. Although the amount of money wasted annually on unreliable thyroid functions tests is staggering, it is trivial in comparison to the suffering or even premature death that may result from a lack of appreciation of a subnormal basal temperature.

Chapter XII

CORRECTING YOUR THYROID DEFICIENCY

IT is necessary for both the patient and the physician to understand the principles of treatment in order to carry out a successful program. The problem is to give enough thyroid to accomplish the desired results and not to give too much which would upset the delicate mechanism that nature uses for regulation. Ordinarily in the normal person a stimulus from the pituitary increases thyroid function when more of its secretion is needed. As soon as the proper amount of thyroid hormone is present in the bloodstream, any excess shuts off the stimulus from the pituitary, and less thyroid hormone is produced. In the normal individual this "feed-back" mechanism regulates the amount of thyroid circulating in the bloodstream in a rather narrow range.

But the patient with chronic symptoms of thyroid deficiency is not normal; the thyroid is incapable of responding to the stimulus from the pituitary. A small quantity of the thyroid hormone must be supplied from the outside, just as extra insulin must be given to the diabetic. If too much extra thyroid is supplied, none is secreted by the patient's own gland; in this situation there is no way the patient can decrease the amount of hormone during periods when less is needed. The patient has a chronic condition of hyperthyroidism. Symptoms of nervousness, inability to sleep the usual number of hours, excess sweating, an elevated temperature, loss of weight, and a variety of other symptoms may develop.

Hence, it is necessary to begin with a small dosage and wait about two months; then, if necessary, the dosage may be raised. The size of the initial dose will vary with the age and size of the individual. Babies under three years of age will not require more than one-quarter grain daily. By the age of six, one-half grain may be used in the beginning, while the teenager or adult may safely be started on one grain daily. In the large male or female, two grains

may be employed, but no more than that dosage should be used until a trial period of observation has passed.

One word of caution: a patient who has had a heart attack should not be given thyroid for at least two months after his attack. Then the initial dose should not exceed one-half grain daily. A little more work is done by the heart during thyroid therapy, and this must increase slowly in those with damage to the heart muscle.

The effect of thyroid therapy begins slowly; no change may be noted for about one month. Between one and two months some of the symptoms begin to subside, and the patient feels better. It is then time to reevaluate the patient's condition and decide if a further increase in dosage is necessary. If all of the symptoms are gone, and performance is satisfactory in work and adjustment to society, the same dosage can be continued until new symptoms indicate that a change should be made. If the serum cholesterol had been found elevated on the initial examination and this has fallen some but not to normal, the dosage may be increased during the second two months if the temperature is still low.

In case it is necessary to elevate the dosage, the amount of the increase again depends upon the age and size of the patient. In children, not more than one-quarter grain should be added to the initial dosage, while in the teenager the increment should be one-half grain, and in the adult as much as one grain should be added. This new dosage is continued for two months, and the patient again reevaluated. The minimum dosage that will convert the subnormal individual into the normal range is the proper dosage. The most common maintenance dosage in adults is two grains; three are sometimes required; rarely are four grains needed.

The basal temperature makes an excellent guide to the proper dosage. It should be low before treatment is started. The normal range of basal temperature is between 97.8 and 98.2 degrees Fahrenheit. Patients registering above this level should be suspected of having an infection or having too much secretion of their own thyroids. During the course of treatment, the basal temperature should not exceed this upper limit of 98.2 unless a sore throat, a cold, or some other infection is present. The patient's gland will not decrease its normal function unless the

temperature is maintained for some time above this level.

In a patient with marked symptoms of thyroid deficiency, the basal temperature may be one, two, or even three degrees below normal. This will usually start to rise during two months of therapy, but still may be below the normal range when all symptoms have diappeared. In the past, the dosage eliminating all of the symptoms has been continued even though the basal temperature was still low. If further experience shows that atherosclerosis is progressing in these individuals, no objection can be raised to increasing the dosage a little as long as the basal temperature does not go above the normal range.

There are many reasons for a patient to be nervous besides too much thyroid secretion. Financial troubles, marital troubles, an unruly teenager, or a variety of tensions may cause the patient to show symptoms similar to those of too much thyroid activity. If the patient is on thyroid therapy at the time, the impression may be gained that the dosage is too high and is responsible for the disturbing symptoms. In such a case, the basal temperature is most helpful; if it is still low, the thyroid should be continued and other adjustments made to the disturbing elements in the daily routine.

Fortunately, large quantities of active thyroid hormone are stored in the glands of packinghouse animals, and such glands are active when ingested by thyroid-deficient patients. It has been demonstrated that fresh thyroid glands will relieve the symptoms, but it is more practical to desiccate and de-fat animal thyroids, standardize the potency, and make the powder into tablets. The fresh glands must be chilled and processed at once or enzyme action apparently destroys some of the active principle. The final product, if prepared properly, may be stored for years without refrigeration; no loss of potency occurs. The desiccated thyroid contains the complete thyroid hormone and is the preparation personally preferred for the treatment of most cases of thyroid deficiency.

Another preparation available on prescription is called Proloid, or thyroglobulin. It contains the natural hormone found in the desiccated thyroid, but some extraneous, inactive proteins have been removed. Claims for superiority are unfounded since a patient eating meat would ingest exactly the same type of

impurities removed from the thyroglobulin during its preparation.

Four synthetic preparations are available on prescription, each of which has activity closely resembling that observed when desiccated thyroid is administered. Some salesmen make exorbitant claims about their product, but careful questioning reveals that crucial tests comparing various preparations on the same patients or on thyroidectomized animals have not been carried out. A suggestion was made to each of the manufacturers of the various preparations that their efforts be pooled and double-blind studies on succeeding generations of thyroidectomized animals be observed. One could then compare the efficacy of each preparation in maintaining normal growth, reproduction, and normal physiology. The suggestion was rejected by the manufacturers of the synthetic compounds.

For years thyroxine was preferred by some clinicians without any proven advantage of the preparation. Two companies have marketed this product under trade names of Synthroid and Letter. Triiodothyronine is sold under the name of Cytomel. Results are obtained more rapidly with the latter preparation than with any of the others, but the effects also disappear more quickly when the medication is stopped. Changes in the metabolic rate should be gradual; the more rapid action has not proven advantageous in my own experience.

Recently two products have appeared in which thyroxine and triiodothyronine have been combined into a single tablet. The ratio of the two is 4 parts of thyroxine to one part of triiodothyronine. The combinations are sold under the names Euthroid and Thyrolar. This proportion is supposedly the same as that found in thyroid glands. However, personal experience of trying to substitute the combination on patients who had been regulated on desiccated thyroid resulted in tachycardia and other symptoms of overdosage in 20 percent of the subjects. It is felt that there is too much triiodothyronine in the combination. It is probably significant that the combination available in Europe contains 5 parts of thyroxine to one of triiodothyronine.

Only two conditions exist in which synthetic preparations have a distinct advantage over reliable desiccated thyroid. The first is in a few rare individuals in whom antibodies to the normal thyroid

hormone develop, rendering the preparation ineffective. This condition is apparently more prevalent in England than in America. The second has not yet occurred, but eventually the demand for thyroid therapy may exceed the supply of fresh glands at the slaughter house. This possibility leaves no doubt that studies should be continued on preparing synthetic replacements. There may be other important iodine-containing components in the thyroid protein which have not been isolated as yet. Certainly it was a mistake when thyroxine was assumed to represent the complete hormone.

From personal experience and from evidence in the literature, only one thyroid preparation cannot be recommended for use in the prevention of cornorary disease. Choloxin, chemically the dextro-isomer of levothyroxine, has been promoted as a safer preparation for lowering the serum cholesterol. When polarized light is passed through a solution of a compound produced in nature, the light is rotated to the left. When similar compounds are synthesized in the laboratory, the chemical formula of the product is identical with that in nature, but the spacing of some of the atoms are different; in half of the synthetic product, polarized light is rotated to the right. The compounds rotating light to the right are usually less active biologically than nature's product.

Salesmanship has exploited the reduced metabolic activity of Choloxin on the assumption that its activity in reducing cholesterol is not impaired to a similar degree. Careful scrutiny of the manufacturer's data does not substantiate the assumption.

On page 714 of the *Physicians' Desk Reference* for 1971, furnished free of charge to all practicing physicians, it is stated by the manufacturer: "Clinical studies have shown that dextrothyroxine exerts one-twentieth to one-tenth the calorigenic activity of levothyroxine." This is true. On page 715 a table is presented showing that 0.1 mg of levothyroxine is approximately equivalent to 1 grain of desiccated thyroid. This is true. On page 714 the recommended dose of Choloxin for lowering serum cholesterol is 4.0 to 8.0 mg daily. No mention is made of the dosage of levothyroxine or desiccated thyroid that would produce a comparable lowering of the serum cholesterol, but the salesmen emphasize that Choloxin is safer.

The results of Choloxin administration (page 715, *Physicians' Desk Reference*) to 406 patients with hypercholesterolemia are very similar to those using desiccated thyroid, as reported by Hurxthal in 1934, by Gildea in 1939, and in unpublished data on several hundred patients personally observed. Very few individuals will require a dosage of 4 grains of desiccated thyroid; most will need considerably less. The metabolic effect of 4 grains of desiccated thyroid would be equal to 0.4 mg of thyroxine or 4.0 mg of Choloxin if the ratio of one-tenth activity were exerted, or 8.0 mg of Choloxin if the ratio were one-twentieth. It is apparent that although Choloxin is one-tenth to one-twentieth as active metabolically as thyroxine, it is also less active in lowering the cholesterol by the same ratio. Greater safety has not been demonstrated.

Personal experience has not indicated that Choloxin is superior to desiccated thyroid in lowering the cholesterol level. Before the compound was marketed, the manufacturer kindly supplied material for personal trial. No agent for the reduction of cholesterol has been effective in every case. Hence, all of those failing to respond to desiccated thyroid were tested for several months on Choloxin in dosages of 8 mg daily or even higher in a few cases. In no instance did the new compound significantly lower the cholesterol below the level attained with the natural hormone.

Repeatedly, some of the patients receiving Choloxin in doses metabolically equivalent to desiccated thyroid developed rapid heart rates and other evidence of intoxication. This was reported to the manufacturer, who stated that perhaps some of the Choloxin was being converted to other more active forms. This seems a plausible explanation in view of Sterling's recent demonstrations that appreciable quantities of thyroxine may be converted to triiodothyronine in normal subjects. This compound is 4 times more active than the original thyroxine.

This variability in activity of Choloxin might prove disastrous if the patient were suffering from undetected coronary disease. Although the manufacturer warns that the compound should not be used in patients with atherosclerosis, nearly half of the sudden deaths from this disease occur without previous warning. This was

clearly illustrated by the collapse of a 28-year-old professional football player during a game in the fall of 1971. If a patient on Choloxin therapy suddenly changed his response from one-twentieth to one-tenth in physiological activity he would increase his effective dose of thyroid hormone by 100 percent. It was clearly demonstrated fifty years ago that such a dosage might be fatal. It appears from present evidence that the dangers of using Choloxin far outweigh any demonstrated advantages.

Chapter XIII

HISTORY PAYS OFF

THE scarcity of new cases of heart disease year after year in the thyroid-treated group left little doubt that this therapy was an effective prophylaxis against public enemy number one. This new part of the program threatened to become the most important phase of the investigation. Belatedly, it was decided to review the early literature on thyroid physiology to see if any support could be found for the new working hypothesis. To my consternation, the old reports indicate that the cause, as well as the cure, for heart attacks was evident years before the disease was recognized as a clinical entity.

The story begins in London during the period in which the American physicians were busily caring for Civil War casualties. Some of the observations of the astute British physicians rival the scrutiny of Sherlock Holmes in his solutions of the legendary crimes in the same city. In a matter of only eighteen years a new disease was recognized, its cause was determined, and effective replacement therapy was found for the deficient ailment.

In 1873 Sir William Gull (33), one of London's leading physicians, reported his observations on 5 patients whom he had studied for several years. He observed changes in adults which previously had been found in children. For centuries a few youngsters were stunted in growth, had a peculiar dull expression, lack of normal intelligence, and an interference with the function of most of their internal organs. These children were called cretins. Gull's adult patients had all of these features except the short stature. He called the condition a "cretinoid" state.

Only five years later, in 1878, Ord (30) reported 5 similar patients, one of whom he had been observing for fifteen years. His major contribution was a detailed autopsy on one of them, and a new name for the disease, "myxedema," which is still used today. So little has been added to the clinical picture in the intervening

ninety-five years that his report will be reviewed in some detail.

The patient was a 54-year-old widow with two normal children. There were no unusual illnesses nor similar cases in her family history. Five years previously she had first noticed fits of shivering while working; on several occasions she had noted blood in her urine. Subsequently, her right hand developed lameness which interfered with her work as a seamstress. She stated that later she became "weak-headed" since she had difficulty in remembering and in keeping her mind clear. She would frequently fall asleep during the day.

This patient developed a general loss of muscular power and had a constant backache. Her speech became slow and difficult. The skin of the entire body became swollen; the face lost its expression. Articles could not be distinguished by touch. She was unable to think or act quickly. Jobs that had required half an hour previously now took two hours. Her gait was slowed; falls were frequent due to lack of muscular coordination.

When this patient was first seen, the physical examination was normal, but within five years the urine showed albumin, the heart was enlarged, the palpable arteries were hardened, the skin temperature consistently ran below normal, and she died, apparently in coma, at the age of 58.

Although the skin was markedly swollen, water did not escape from a cut surface as it does in cases of edema due to kidney failure. Chemical analysis revealed an excess of a jelly-like mucin throughout the tissues; hence, Ord coined the term "myxedema" for the disease, as suggested by the mucus and the swelling. Unfortunately, this designation has persisted although it indicates only a disease of the skin while actually all of the other tissues in the body are also afflicted.

At autopsy the chest, the abdomen, and the sac around the heart contained much fluid; the lungs were emphysematous; the heart was markedly enlarged and its muscular walls thick; the arteries were everywhere thickened with severe atherosclerosis; the kidneys were wasted and granular with large atheromatous arteries; and the arteries of the brain showed considerable degeneration. The thyroid was almost completely destroyed, thus indicating that the condition was due to thyroid failure. Cretins

were known to lack thyroid hormone.

In addition to the skin, the connective tissues, even in the arterial wall, showed mucus-yielding deposits causing swelling and interfering with function. This material appeared to be the result of degeneration since it did not take the stains as living tissues do. The extensive atherosclerosis in the lumen of the arteries undoubtedly would have led to a heart attack had not the coma or some infection shortened her life.

It is well to bear in mind that this case of advanced atherosclerosis occurred years before the plush diets, the sedentary living, cigarette smoking, and atmosphere pollutants entered the picture. In the absence of the environmental factors, hardening of the arteries developed in those surviving into adult life, if the thyroid function failed.

The London Clinical Society was intrigued with the widespread effects of thyroid failure and appointed a commission of thirteen investigators to study the disease in more detail. Five years later, in 1888, the committee published a report (34) of over two hundred pages in a supplement to Volume 21. This first crash-program was a masterpiece, but unfortunately it has been forgotten and its significance unappreciated. Heart attacks had not been recognized, and attempts at treatment did not arise until twenty-four years later. A new generation was not acquainted with the work of the old masters.

The commission reviewed over 100 cases of myxedema that had appeared in the literature since Gull's description fifteen years earlier. Although, as with other diseases, all of the symptoms and findings are not found in each patient, no gross errors appeared in the reports of Gull and Ord. Dr. Victor Horsley was requested to attempt production of the disease in experimental animals; he was successful in several species. Only the results on monkeys will be mentioned since this species is closely related to man.

Within seven days after removal of the thyroid gland in monkeys, the connective tissues in the blood vessels developed deposits of mucin-yielding compounds which led to mucoid degeneration followed by fibrous tissue. It will be seen presently that this same process is the initial lesion in arteries leading to atherosclerosis in all species. Had heart attacks been prevalent at

the time of Horsley's dramatic demonstration, the "riddle of heart attacks" would have been solved many years ago.

The early attempts to relieve thyroid deficiencies were directed towards transplanting thyroid glands from other individuals or from animals into the hypothyroid patients. The same problem of tissue rejection plaguing heart transplants today defeated the temporary improvement. Yet only three years after publication of the commission's report, successful replacement of the thyroid hormone was accomplished by Murray (35) in 1891. He made a glycerine extract of fresh thyroid tissue and injected the crude juice into patients. Complete relief of all the symptoms could be achieved by this procedure, but the major problem was deterioration of the preparation.

Soon it was found that eating the fresh thyroid glands would also furnish the vital hormone; again, it was necessary to prevent decomposition of the fresh meat. The final step was to de-fat and dry the fresh glands; this process did not destroy the active principle; desiccated thyroid is one of the most successful medications still on the market today.

The efficacy of the thyroid hormone in curing the diverse pathology observed in the first case autopsied by Dr. Ord is proven by Murray's first recipient, in 1891, who remained in good health until she died nineteen years later at the age of 72. During the interval she attempted to stop medication several times but promptly developed her original symptoms. That she survived a normal lifespan certainly indicates that atherosclerosis was being averted.

While the British were establishing the cause and the cure of myxedema, progress in the physiology of the thyroid was progressing in other countries. In 1883 Kocher (36), a surgeon in Switzerland, improved the technique for removing huge goiters which were suffocating patients. About one-third of those undergoing complete thyroidectomy developed profound symptoms identical with those described by Gull and Ord. Billroth (37) was the leading surgeon in Vienna at the time; he soon confirmed the observations of Kocher.

The routine autopsies in Vienna quickly substantiated the arterial damage observed in Ord's autopsied case of myxedema. It

became evident that loss of thyroid hormone led to premature hardening of the arteries. One of Billroth's assistants, von Eiselsberg, was so intrigued by this phase of the problem that he began to reproduce the condition in experimental animals. In 1895 he reported (38) that thyroidectomy in sheep or goats led to atherosclerosis in the arteries, including those of the heart. A few years later Pick and Pineless (39), also in Vienna, confirmed these results and found that thyroid therapy would prevent the premature arterial damage.

It is apparent that during the last century premature atherosclerosis was demonstrated in patients suffering from hypothyroidism; thyroid therapy abolished the symptoms of the disease; the condition could be demonstrated in experimental animals simply by removing the thyroid gland. Why has this information been neglected for so long? Unfortunately these observations preceded our knowledge of heart attacks by many years. There was no practical application at the time; "another rose was born to blush unseen." It was not until 1912 that Herrick (14) suggested that something might be done for the patient collapsing with atherosclerosis in the arteries to the heart. By this time the role of the thyroid in hardening of the arteries had been forgotten. A confusing series of circumstances further delayed the emergence of the truth; these will be detailed in the next chapter.

Chapter XIV

THE COMEDY OF ERRORS

BEFORE sound was added to the motion picture screen, the Mack Sennett silent comedies featured the villain escaping from the sheriff by going around a revolving door or disappearing around a turn in the road. For many years thyroid deficiency has escaped detection as the culprit in heart attacks by the same narrow margin; evidence incriminating the thyroid has repeatedly appeared, but some other interpretation has been placed on the facts. Cholesterol was exonerated as the cause of atherosclerosis long before heart attacks became important; the evidence was buried and forgotten.

The proof that cholesterol was a fellow traveler and not the murderer appeared on my birth date (but I do not recall the incident); it occurred exactly forty-eight years before I was born. Rudolph Virchow (40), professor of pathology in Berlin and the father of this new science, gave a lecture and a demonstration from autopsy material showing clearly that degeneration began in the connective tissue of the blood vessels before cholesterol appeared at the site. The next step was an accumulation of fat droplets, and the third step was appearance of cholesterol liberated in abnormal amounts.

By the time fat droplets, the source of the cholesterol, began to appear, circulation to this area was markedly impeded; fresh nourishment could not get into the area and waste products could not be carried away. Virchow looked upon the cholesterol as a belated secretory product of fatty degeneration. In the same lecture he demonstrated identical changes occurring in a strip of heart muscle from an autopsy on a patient with a crooked spine. The heart had been pressed against the chest wall, impairing the circulation of the heart muscle. Exactly the same changes occurred in the area lacking blood that were seen in atherosclerosis of the blood vessels. The heart muscle on either side of the pressure point

was quite normal and did not show deposits of cholesterol; the latter was present in the dying area.

Repeatedly in the last one hundred years pathologists have confirmed the observations of Virchow: cholesterol is not present in the beginning of the degenerative process but only appears after the fat droplets accumulate. It was fifty-five years later that Anitschkow (7) fed rabbits huge quantities of cholesterol and produced atherosclerosis in them. Apparently he was not acquainted with Virchow's work and naturally felt that the cholesterol caused the degeneration. Obviously he was also unaware of von Eiselsberg's (38) work on the sheep in Vienna, or he would have realized that exactly the same atherosclerosis could be produced by thyroidectomy without any cholesterol in the diet. We can blame his error on a lack of communications.

It will be recalled from Chapter 4 that feeding cholesterol to rabbits lowers their metabolism as effectively as removing the thyroids. Actually, Anitschkow did not prove that cholesterol causes atherosclerosis, but confirmed von Eiselsberg's work that another herbiverous animal behaves similar to the sheep. However, Anitschkow's co-workers were soon impressed by the role of the thyroid. In 1927 Friedland (41) suggested using thyroid therapy as a prophylaxis against atherosclerosis. Apparently the Russian laboratory was impressed with the importance of thyroid deficiency rather than the role of the cholesterol. On the contrary, the Americans retained the cholesterol theory.

By 1934 Dr. T. Leary (42), the Boston Medical Examiner, had accumulated 9 deaths from heart attacks in patients under 40 years of age. His autopsy studies were very thorough. He even repeated the cholesterol feeding to rabbits. He was satisfied that the process was very similar in both species. Although he did not mention Virchow's observations of 1858, he did state that fat was not deposited in connective tissues until mucoid degeneration had occurred. He did not find the early degenerative changes in patients dying of heart attacks, but only in babies a few weeks old dying from congenital heart disease.

Leary had no explanation for the initiation of mucoid degeneration. Apparently he was unaware of the *British Commission Report on Myxedema* in 1888. There he would have found

mucoid degeneration common in cases of myxedema, and also the same degenerative process in the arteries of monkeys one week after thyroidectomy. He was aware that the thyroid was implicated in some manner. In a vigorous defense (43) of the cholesterol theory he concluded that atherosclerosis is a disease of cholesterol metabolism, that stress appears to be responsible for localization, and that aberrations in thyroid function appear to be factors in preparing the internal ground substance for deposit of cholesterol. Obviously, he was impressed with the importance of thyroid deficiency, but he could not abandon the cholesterol theory.

Undoubtedly his keen observations and his stature as a pathologist have been instrumental in keeping the attention of the Boston scientists focused on cholesterol. In retrospect, it is easy to see how the gap in international science, coupled with the epidemiological evidence that heart attacks were rare in underdeveloped countries, kept the cholesterol pot boiling. However, this does not excuse therapeutic errors in the use of thyroid in heart disease, as illustrated in a later paragraph.

Although many autopsies on cases of myxedema since Ord's original description in 1878 had indicated heart failure, it was not until 1918 that Zondek's (44) report focused attention on thyroid deficiency and the circulatory system. He found that some bedridden cases of heart failure did not respond to digitalis, yet thyroid therapy returned them to work in a comparatively short time. He called this clinical entity "myxedema heart." All of his cases had the facial appearance of myxedema. Unfortunately, many patients may have evidence of heart failure due to thyroid deficiency without characteristic changes in the skin.

Clinicians from all over the world soon confirmed Zondek's observation; Christian's (45) results are typical of many others. In 1925 he reported 6 cases, one of whom died suddenly before therapy could be started. An autopsy revealed that the coronary arteries were markedly narrowed due to atherosclerosis. In other words, myxedema heart was identical with coronary disease clinically and at autopsy. One patient was 73 years old when heart failure became evident. She had been successfully treated for thyroid deficiency for twenty-five years and developed heart

failure only when she stopped her thyroid therapy. The resumption of two grains daily cured the condition.

Christian found that many physicians were starting patients on too large a dosage of thyroid. In treating heart failure with digitalis, it had been customary to rapidly saturate the patients with the drug, then cut the dosage back for maintenance. The same was tried with thyroid, but suddenly increasing the work of the heart with too large a dose of thyroid produced angina and, in a few cases, death. Using a dosage of 1 grain daily and slowly increasing it to 2 grains gave satisfactory results without undesirable side-effects.

In spite of similar reports from other investigators as late as 1938, a stern warning appeared (46) about the dangers of thyroid therapy in cases of coronary disease. The author collected 8 deaths from the literature and added one of his own that occurred after thyroid therapy was started. Personal review of each report revealed that the minimum dosage of thyroid employed was 4 grains daily and the maximum was 30 grains. It is obvious that this author and a few others had failed to follow the advice of their peers. Subsequently, many physicians refused to consider the use of thyroid in heart disease because they thought it too dangerous. The report did not point out the hundreds of patients with heart disease who had lost their angina and were cured with physiological doses of thyroid. It only emphasized 9 cases of therapeutic errors. If digitalis had been used in comparable overdosage, far more than 9 deaths would have resulted, yet digitalis, like thyroid, is very useful when used properly. A mistake in the field of medicine sometimes takes years for correction.

Another error was made in the dosage of thyroid necessary to reduce the serum cholesterol and other lipids of the blood. Hurxthal (47) had shown that the serum cholesterol of the blood was elevated in hypothyroidism and was low in hyperthroidism. In 1939 Gildea (48) showed that the lipoproteins and the triglycerides were also elevated in hypothyroidism. Doses of one or two grains daily of thyroid would restore a normal lipid pattern. This information again preceded its importance by several years.

By 1954 Gofman and his associates (49) had decided that elevated beta-lipoproteins were a major factor in coronary disease.

They tested the ability of thyroid administration to keep the cholesterol and lipoproteins below normal in schizophrenic patients who did not suffer from thyroid deficiency. They were justified in using such patients, and found that about 5 grains daily were necessary to completely suppress the normal thyroid function. It has long been known that normal individuals can tolerate more thyroid than myxedema cases since the normal thyroid stops functioning in the presence of too much hormone from the outside.

But the error came when the clinicians began treating cases of elevated cholesterol and other fats with 5 grains of desiccated thyroid. These patients were not normal; many of them were suffering from coronary heart disease. At once angina and other evidence of overdosage appeared just as it had in myxedema heart cases thirty years earlier. Instead of realizing their mistake in dosage, Moses (50), Oliver (51), and Owen (52) promptly concluded that thyroid therapy could not be used. Had they been acquainted with Gildea's work, with numerous reports on treatment of myxedema heart, or even with the details of Gofman's report, they would have had no trouble with one or two grains of thyroid daily. Thyroid therapy had another "black eye" from a therapeutic error; progress was again delayed.

It was the undesirable side-effects noted above that led investigators to try derivatives of thyroxine with less metabolic activity for lowering serum cholesterol. The error of using dextrothyroxine was pointed out in the chapter on treatment. The comedy of errors loses its humor when it is realized that thousands of premature heart attacks might have been avoided if the scientists had heeded the advice of Friedland in 1927.

No longer can the defenders of cholesterol be excused on a credibility gap. They have developed an interesting technique encountered recently in a couple of deaf-mutes who communicate only by lipreading. If one of them wishes to stop an argument, the head is turned away so the lips of the other are not visible. Those defending the cholesterol theory have turned their heads from the reports which leave little doubt that thyroid therapy is efficacious in coronary disease.

Fortunately all of the work on thyroid has not been full of

errors. In 1951 the late Dr. William B. Kountz (53) published a short monograph entitled *Thyroid Function and its Possible Role in Vascular Degeneration.* After reviewing much of the early evidence linking the two conditions, he combined observations from his private practice with some from infirmary patients at Washington University in St. Louis. Three age-groups were included: the first was business men with an average age of 55 years, the second was outpatients at the infirmary whose ages averaged 61 years, and the third group, confined to the infirmary, whose average age was 67 years. The 3 groups totaled 288 patients.

Each patient had a low basal metabolic rate and many had high serum cholesterol levels. The first group had very little evidence of atherosclerosis, the second group included many with moderate degrees of cardiovascular damage, while in the third group each individual had evidence of advanced disease of the blood vessels. Some in each group were treated with thyroid therapy while the others were kept as controls. For over five years observations were carried out, and the results listed in terms of death from heart attacks or strokes.

There were no deaths among the younger group receiving thyroid therapy, while 15 percent of the controls had fatal vascular accidents. As age progressed, the efficacy of the thyroid therapy was more apparent. In the second group 3 percent of the thyroid-treated individuals died while the mortality of the controls was 19 percent. Even among the advanced age group where death might be expected at any time, fatalities were one-half as frequent among the thyroid-treated patients.

These striking results on the human confirm the delay in atherosclerosis observed in experimental animals over thirty years earlier. Apparently the process can be slowed down at any age, but obviously the time to begin therapy is in the young. Kountz's data in 1951 offered a rational explanation for the absence of any heart attacks among young individuals who had been personally treated with thyroid therapy between 1937 and 1950 (Chapter 9). His results clearly indicated that the observations should be continued; they played no small role in the decision to enter the field of atherosclerosis. The results in Chapter 10 more than justify the

twenty years of additional effort.

Before any personal publication on this subject had appeared, others began to substantiate Kountz's conclusions. Isreal (54) was the first to confirm that thyroid therapy was efficacious in patients with coronary disease. Several personal preliminary reports have added to the evidence, and more recently, Wren's (55) controlled studies on older patients with atherosclerosis also indicate that thyroid therapy offers hope. It is regrettable that the truth has been slow in emerging, but scientists are first of all human; it is never too late to correct mistakes.

If there is acceptance to the theory that premature atherosclerosis develops in thyroid-deficient patients, a new question is apparent at once. How did our modern scientific society accumulate so many cases of a single disease? The answer seems simple; it does not appear to be pollution. One explanation follows in the next chapter.

Chapter XV

A BIT OF PHILOSOPHY

IN the previous chapters convincing evidence has been presented indicating that hypothyroidism predisposes to atherosclerosis. If the thyroid deficiency were responsible for the rise in heart attacks, has there been a marked increase in patients with low thyroid function in recent years? If so, what has produced this change? If there has been no change in hypothyroidism, why did it not cause heart attacks in the last century rather than appear at present? If there have been so many of these cases around, where did they come from? These and a host of other questions must be answered before a theory can connect this disorder with the rise in heart disease.

Beginning with the last question, the origin of hypothyroidism has been very clearly established. From the beginning of medical history goiters have been known throughout the world. Modern experimentation has proven that this enlargement is due to insufficient iodine in the soil and drinking water. The extreme cases of cretinism have been sterile and have not produced their kind, but milder deficiencies have been passed on through successive generations. The familial occurrence of this disorder has been observed repeatedly.

One might expect natural selection to blend the hypothyroid population with normal individuals, and over centuries the low metabolism cases would disappear. This brings up some interesting philosophy. Experience over many years has revealed that one thyroid-deficient patient marries another one, thereby keeping the breed relatively pure and perpetuating it. This fantastic idea is not as unreasonable as it sounds.

Unless the courtship is a whirlwind affair, natural selection will tend to pair off individuals having similar amounts of energy. The low-thyroid individual with poor circulation, fatigue, and a requirement for additional sleep could not accompany a date to a

dance or other entertainment several nights each week and still function the next day. If a normal individual were attracted to such a person, he would soon drop the old "stick-in-the-mud."

On the other hand, if two individuals with a marked difference in energy endowments did marry, some of them would end up in a divorce court. This was first brought to my attention by a man who came into the clinic 100 pounds overweight and who had just enough energy to get through the day's work. An alteration in his diet and some thyroid therapy, which was needed for other reasons, resulted in an energetic, attractive male nine months later. George returned complaining that something was wrong with his wife; she was tired and cross and was unwilling to go out in the evening. When George was reminded that he used to come home from work, eat his dinner, read the newspaper, and promptly go to bed, he realized that their incompatibility had arisen from changing his energy level. Nature had thrown them together originally, and if they were to enjoy life, the doctor must be called upon to treat both of them in order to maintain a balanced team.

Thus, the source of the hypothyroid patients is apparent. However, why did they wait until the twentieth century to develop heart attacks? The answer is, "They didn't." A few of them had been occurring for at least two hundred years; they were not recognized as such. The chapter on symptoms of the disease gives a rational explanation for the phenomenal rise during recent years. It will be recalled that an outstanding symptom of thyroid deficiency is a susceptibility to infections. During the previous centuries over half of the population died from a multitude of infectious diseases before they ever approached the age at which heart attacks might be expected.

The first major change in death patterns occurred during the latter part of the nineteenth century, when the patients with tuberculosis were segregated and kept in bed. The carnage from this disease began to decline. It was only then that pathologists in Europe began to see regularly autopsy evidence of occlusion of the arteries supplying blood to the heart. These observations preceded the mild change in diet that has occurred, the cigarette, the automobile, and the modern industrial pollution. This was the start of the "new population" discussed in Chapter I.

How frequent is hypothyroidism today? Without accurate tests for measuring thyroid function, it is impossible to make an estimate. It is apparent that each individual surviving premature death from an infectious disease adds one more to a growing population whose past history included an outstanding symptom of thyroid deficiency. Eventually half of the surviving adults will owe their longevity to the escape of infectious deaths. Will all of these individuals be suffering from hypothyroidism? The question is purely academic; forty years of experience indicates that they still retain other symptoms of the disorder. Before antibiotics appeared, thyroid therapy markedly reduced the carnage from infectious diseases in my practice. The other symptoms are still responding to the same treatment. The unreliable thyroid-function tests may not confirm the diagnosis, but as long as the basal temperature is subnormal, thyroid therapy will add substantially to the health of the patient.

Chapter XVI

RECAPITULATION: THEORIES MUST FIT THE FACTS

THE riddle of heart attacks is solved. Autopsy studies clearly show that man has changed more than the environment. Some of those surviving premature deaths from infections are now dying from heart attacks, lung cancer, and emphysema. Most of the heart attacks occur in old age and are due to fair wear and tear on the arteries. The confusion arose when cholesterol, one of man's best friends, was falsely accused of being the culprit in heart attacks. Efforts to prove the impossible led to erroneous interpretations of many facts.

The cholesterol theory was founded on the observation that atherosclerosis developed in rabbits fed toxic doses of cholesterol. It was strengthened by the rarity of heart attacks in countries not eating cholesterol-containing foods. It was allegedly proven by the drop in heart attacks in Europe during World War II and their prompt rise after the war. Cholesterol foods were in short supply during the conflict.

This circumstantial evidence has not withstood the accumulation of more facts. Many species of animals, including man, do not develop atherosclerosis when fed reasonable doses of cholesterol. Even some strains of rabbits are immune to cholesterol-feeding until their thyroid function is reduced. In all species of rabbits, simultaneous thyroid administration with the cholesterol prevents damage to the arteries. In those rabbits developing atherosclerosis from cholesterol feeding, the metabolism falls comparable to that seen by removing the thyroid gland before the atherosclerosis appears. It is obvious from the rabbit experiments that not cholesterol but low thyroid function is responsible for hardening of the arteries.

This was conclusively proven eighteen years before the rabbit experiments by removing the thyroid gland from sheep; the same type of atherosclerosis promptly appeared. The sheep, like the

rabbit, never voluntarily eats cholesterol-containing foods. Furthermore, years before cholesterol was implicated, the autopsies in Vienna revealed that thyroidectomy in man led to premature atherosclerosis.

Autopsy studies have also forced a new interpretation for the epidemiological data supporting the cholesterol theory. In countries having few heart attacks, children and young adults have more damage to the arteries of their hearts than similar-aged groups in countries eating cholesterol foods. Obviously, low cholesterol diets do not prevent atherosclerosis. But the rarity of heart attacks still had to be explained. The autopsies answered this question. The countries having few heart attacks have a high incidence of infectious diseases, including tuberculosis, which remove the candidates for heart attacks before fatal damage to the arteries can occur.

Autopsy protocols prepared during World War II exploded the "alleged" proof of the cholesterol theory. The reduction in cholesterol intake during the war did not prevent atherosclerosis; actually, damage to the arteries was fourfold greater than either before or after the war. Heart attacks went down during the war because a marked rise in tuberculosis and other infectious diseases was eliminating that segment of the population susceptible to heart disease. It is apparent that no substantial evidence supports the cholesterol theory.

During the interval in which the cholesterol theory was riding the waves of notoriety to its doom, concrete evidence from many sources was accumulating indicating that the thyroid gland was implicated in hardening of the arteries. All species of animals, including man, readily develop atherosclerosis if the thyroid function is reduced. By accident, it was discovered that thyroid therapy to young people over several years prevented the appearance of heart attacks in this group. An additional twenty-year study revealed that treating high-risk patients with only thyroid prevented 94 percent of the expected heart attacks. Other investigators have demonstrated that patients with advanced atherosclerosis are materially benefited by thyroid therapy.

The trial of cholesterol versus the people has come to an end; the evidence is now turned over to the jury, namely you. Only you

can decide if you want to continue with an abnormal diet, and with a change in other living habits in a futile effort to avoid a premature heart attack. If you think cholesterol has not had a fair trial, check the disaster to the dairy industry and the fortunes that have been made with the unsaturated fats. In spite of heroic sacrifices, there has been no significant drop in heart attacks during the last twenty years.

Your other alternative is to take your basal temperature and find an enlightened physician willing to cooperate in a new program. If your temperature is subnormal, the odds are far higher than you can get in Las Vagas that some thyroid therapy will not only avoid a premature heart attack but will also prevent many other complications that accompany the aging process.

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