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# Body temperature in health and disease

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# Preface

Body temperature is universally accepted as the most common indicator of the normal or pathological state of the body. Doctors and laymen alike check the temperature at the earliest complaint of an illness, often not knowing the normal for that particular individual. A negative temperature finding, however, is very significant and eliminates a large number of possibilities.

Mammals and birds alike are homoiothermic, and that to a very fine degree. It seems quite amazing to me that we can survive such extremes of environmental temperature and humidity with such small variations in body temperature and with those variations being regulated back to within a small fraction of a degree of normal in such a short period of time. Year after year, winter and summer, the body generates and dissipates heat with only slight variations in the resultant. One would expect a very complicated and very intricate mechanism to be necessary for the direction of a machine composed of such complex chemical and physical factors as the human body; and such is the case. Because of this complexity and intricacy, the physiology of body temperature is not well understood at the present time.

Stable and homoiothermic though it may be, body temperature still displays numerous variables of the so-called normal--some being pathological and others being physiological, according to the individual case. For centuries, body temperature has been called the primary manifestation of health and disease, as the case may be; yet it is still a baffling problem at times.

Body temperature is not only a diagnostic sign, but when understood, it is also an index to the prognosis and progress of disease. There are specific types and patterns of fever, which are significant and indicative of specific bodily conditions and pathology, and which, therefore, confirm or deny other findings. As the disease progresses for better or worse, the temperature also changes. Sometimes the fever is beneficial; at other times, it merely adds discomfort and perplexities to a diseased condition.

The purpose of this thesis, then, is an attempt to explain the mechanism of normal body temperature, to bring to light the normal and its variations, to present the abnormal, and to correlate abnormal body temperature findings with various physiological disturbances.

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# I

## Physiology of the Mechanism of Temperature Regulation

Body temperature is the result of the balance or lack of balance, as the case may be, of two factors--heat production against heat dissipation. These factors are physiologically subordinate to and relegated by the central nervous system. In health, this adjustment is extremely fine, whereas in disease, it displays a much greater variation. A slight increase or decrease in one factor prompts a counteraction by the other factor if the balance is to be maintained. There are many pathological conditions that may cause a loss of balance in the factors of heat production and heat dissipation. The finesse of this balance can be better realized when we consider that failure to dissipate ten per cent of the daily heat production, or about two-hundred-thirty Calories, would result in a fever of one-hundred-six degrees Fahrenheit (Du Bois, 1937).

### HEAT PRODUCTION.

Heat production, of course, is chemical and results from the chemical action of compounds taken into the body, which are oxidized to heat and waste products largely by means of the muscles and liver. For example,

carbohydrates, proteins, and fats, either directly or indirectly, are changed to glucose and are eventually metabolized to produce heat, carbon dioxide, water, and nitrogenous and other waste products. In other words, body heat results from the combustion of food within the body, and the principal site of this combustion is the skeletal muscle and the glandular organs, such as the liver and, to a lesser extent, the kidneys. A negligible amount of heat is derived by radiation from warmer objects; but this occurs only under special circumstances, such as from hot water bottles, hot pads, and so on.

Using cats as the experimental animals, it has been demonstrated that when an animal is chilled, there is, at first, only a slight increase in the number of action currents in the muscle fibers. If this does not cause contraction of enough fibers to raise the heat production to balance heat dissipation, the number of action currents becomes increased until groups of fibers eventually contract synchronously to produce the so-called goose pimples (Burton, 1937). This condition may increase to the extent of shivering.

When skeletal muscles are paralyzed by large doses of curare (Reichert, 1891), the animal loses its power to maintain body temperature in a varying environment

and becomes more or less poikilothermic, because the mechanism of heat production has been paralyzed. Small doses may cause, first, a rise and, later, a fall in body temperature. The significance of the muscle action is also indicated by the fact that heat production can be increased from sixty Calories per hour to more than eight hundred Calories per hour by means of violent exercise.

Furthermore, Dworkin (1930) found that shivering was under the control of the hypothalamus. By cooling the hypothalamus, shivering could be produced in the presence of hyperthermia; and, conversely, shivering could be stopped by warming that area of the central nervous system. This experiment was verified by Barcroft and Izquierdo (1931).

HEAT DISSIPATION.

Heat dissipation is largely a physical process, involving the factors of radiation, convection, conduction, and evaporation of water from the skin and lungs. These factors account for ninety-six per cent of the heat loss of the body. Raising the temperature of the inspired air accounts for about two to three per cent of the heat lost, while the loss due to urine and feces and to food intake is about one per cent of the

total of around three thousand Calories daily. Every gram of water vaporized from the skin withdraws 0.58 Calories through the latent heat of vaporization. It might be added, however, that the rate of vaporization is a highly variable factor and is affected by the humidity and surrounding air currents. Also of importance is the insulation or the covering of the patient when these various factors are in operation.

Heat dissipation is further affected by the superficial vasodilatation and by the heat delivered by the blood circulating through these parts and the lungs. When we become excited or tense, our muscles put out more heat, metabolism increases, and, at the same time, we experience a vasodilatation in the muscles, with splanchnic constriction. The heart rate increases, and if the heat production is too great for the rate of dissipation, we may start to perspire and to breathe more deeply and more rapidly.

Two systems which are parallel in their purpose and ultimate end with regard to heat production and dissipation are adrenalin (chemical) and sympathetic stimulation. These two systems keep the body balanced in its temperature and ready for action. This, however, implies another important factor in temperature balance, that of correlation of heat production and dissipation.

HEAT CONTROL CENTERS.

What actually maintains the balance of heat production against heat dissipation has been a question of considerable experiment and theoretical explanation until the early part of this century. Many scientists held the opinion that body temperature was not ascribed to a specific center, but was, rather, the result of various physico-chemical factors, as were the blood-calcium level and blood acidity. However, modern literature dealing with temperature control becomes more and more concordant in ascribing the main function of this control to the hypothalamus.

Tscheschichin (1866) was among the first to observe a variation in temperature following injury to various parts of the brain tissue of the rabbit. Aronsohn and Sachs (1876) first described the heat puncture caused by puncturing or otherwise injuring or stimulating the medial side of the corpus striatum with heat. They reported a rise of 1.7 to 2.4 degrees Centigrade, which lasted for several days. These observations led to the theory that there existed in the brains of birds and mammals a special "heat center", which automatically regulated the heat production and dissipation in such a way as to maintain a constant body temperature. Subsequent

investigators confirmed the existence of various other "heat centers". Ott (1884) located the center in the neighborhood of the corpus striatum, optic thalamus, tuber cinereum, and pons.

Removal of the cortex and thalamus does not destroy the controlling mechanism so long as the hypothalamus remains intact. Transection through the midbrain at the level of the superior colliculi or any level posterior down to the lower cervical portion of the cord renders the animal poikilothermic. Section of the cord in the upper thoracic region, i. e., above the level of the outflow of the greater part of the sympathetic fibers, abolishes physical heat regulation, but leaves chemical heat regulation, for the most part, at least, intact, due to the fact that the muscles of the fore part of the body are in communication with the central nervous system (fig. 1). Therefore, section through the brain stem indicates that the main center or centers for heat regulation must lie anterior to the superior colliculi. Destruction of this region makes it impossible to maintain body temperature in cold environments, because heat dissipation is released and is evidenced by panting and vasodilatation (Gardiner, 1912).

Kellar and Hare (1931) found that puncture injuries in the thalamus, hypothalamus, corpus striatum, and

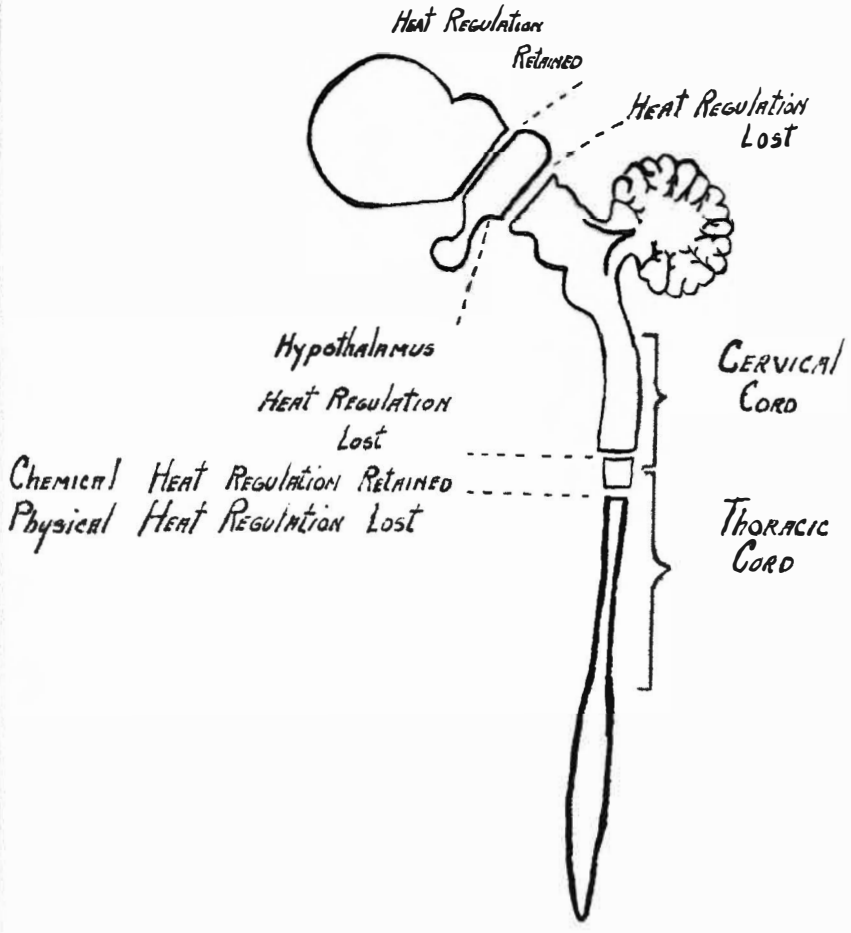


Fig. 1. Diagram to illustrate the nervous control of the heat-regulating mechanisms. (Best and Taylor).

septum pellucidum might cause derangements of temperature control. A number of experiments have been performed on that region; but it was not until 1933 that the full significance of the hypothalamus and corpus striatum was realized. In that year, Bazett, Alpers, and Erb (1933), working with cats, limited the heat control centers to the hypothalamus. They found that the presence or absence of temperature control appeared to be associated with the preservation of the hypothalamus just cephalic to the corpora mammillaria; the area included the nuclei surrounding the walls of the third ventricle and the infundibular nuclei. The experiment was related to the sweating and vasodilatation part of the raising and lowering of body temperature. The experimental animals, however, did not show a normal hyperpnea when exposed to excessive heat.

Ranson and Ingram (1935), using the rhesus monkey, were able to produce small, sharply localized lesions of the hypothalamic region by means of a small electrode. Nine of the animals lost the capacity to prevent body temperature from falling below normal in an environment of eighty-six degrees Fahrenheit, or below normal temperature.

Haertig and Masserman (1940) reported experimental data obtained from operations performed on a series of

forty cats. Hypothalamic lesions were produced in each of the forty animals, and the conclusions of this study may be summarized as follows:

1. The animals with lesions in the rostral portion of the hypothalamus retained the ability to prevent abnormal depressions of temperature.

2. Those with caudal lesions displayed an occasional disturbance of temperature regulation.

3. Those with lesions of the middle hypothalamus were markedly poikilothermic, but could not maintain hyperthermia under fluctuating environmental conditions.

These conclusions, however, are not as accurate as they might appear. The validity of the experiment was somewhat unbalanced, due to the extreme sensitivity of the temperature centers, the smallness of the various parts of the hypothalamus, and the delicate methods required for the preventing of too much post-traumatic reaction and, at the same time, for the producing of the desired physiological effects.

Ranson, in 1940, located more precisely the thermoregulatory centers. Basing his views on the results of his experiments on cats and monkeys, he placed the controlling centers in the preoptic and supraoptic regions between the anterior commissure and the optic chiasma.

Heating this area caused sweating and panting, or rapid breathing, and falling of body temperature toward environmental levels. Destructive lesions of the area caused a hyperthermia, which ordinarily would not have occurred in similar environments. Sweating and panting did not occur, although the animals were exposed to temperatures up to one-hundred-six degrees Fahrenheit. Ranson and his associates thus concluded that the centers controlling heat production and heat conservation, enabling the animals to maintain normal body temperatures when exposed to cold, were located in the caudal part of the lateral hypothalamus and seemed to be identical with the sympathetic center. From observations of patients with brain lesions involving the base of the brain, it also appears likely that the heat control centers in man are situated as described by Ranson for animals.

The temperature centers of the central nervous system are affected in two ways--reflexly from the skin and by the temperature of the blood flowing through the centers. Jelsma (1930) observed an antagonism between the vertebral and carotid circulations with respect to control of the heat regulating centers. When the vertebral arteries of a dog were heated, or the carotids cooled, the following phenomena were recorded: shivering,

peripheral vasoconstriction, hyperventilation, and dyspnea. With chilling of the vertebrals or heating the carotids, somewhat different phenomena were observed; namely, peripheral vasodilatation, shallow respirations, and vomiting. The rectal temperature, it was found, varied in the same direction as that of the medulla, and in a direction opposite to that of the basal ganglia.

The posterior hypothalamic center apparently exerts its controlling influence upon temperature through the transmission of impulses, via the sympathetic, to the cutaneous vessels, sweat glands, and pilomotor muscles, and via somatic fibers, to produce shivering; removal of the sympathetic renders the animal unduly susceptible to cold. When the temperature is rising rapidly, sympathetic activity is evidenced by cutaneous vasoconstriction, dilated pupils, and erection of hair. During a rapid fall in temperature, parasympathetic activity is manifested by cutaneous vasodilatation and constricted pupils. Sympatheticotonic drugs, such as ephedrine in large doses, will cause a rise in body temperature, and vice versa.

BODY TEMPERATURE AND THE ENDOCRINES.

Some years ago it was shown that adrenalectomized

rats could not survive in a low environmental temperature (Kendall, 1941). The administration of extracts of the adrenal cortex or the purified crystalline hormones permitted such animals to survive indefinitely. For this action, the cortical compounds, which have an oxygen on carbon eleven and which affect carbohydrate metabolism, and the amorphous fraction of the cortical extract, which does not have any effect on carbohydrate metabolism, were about equally effective in preventing death of the animals. This suggests that the essential effect is produced through a control of the distribution of electrolytes and water and through maintenance of a normal volume of blood.

The thyroid is also very important in heat production. Thyroid hormone is essential to cell metabolism. The cells metabolize more quickly and the combustion of foodstuffs is more rapid when the thyroid hormone is present than when it is absent (Canzanelli, 1933). Muscle tone is increased and a fine tremor occurs with an excessive amount of thyroid secretion. These factors add up to greater heat production, which, with a nearly normal heat-dissipating mechanism, leaves the individual with a variable degree of fever or temperature above normal.

The anterior pituitary also puts out a thyrotropic hormone, without which the thyroid would become atrophic and body metabolism would become diminished and myxedematous. Then, too, there is a posterior pituitary antidiuretic substance which prevents excessive diuresis, or water loss (Gilman, 1937). The water loss would, of course, cause dehydration with a consequent fever on that basis. The active antidiuretic part of pituitrin is the pitressin, or the pressor principle, which is active at the loup of Henle in the reabsorption of water (Rosenfield, 1940). Thus we see that these glands are active in maintaining metabolism and water balance, and that this metabolism and water and salt balance are geared to a very definite body temperature.

The endocrines are obviously involved in the regulation of body temperature. The adrenals are observed to give very rapid, but short, calorigenic effects, whereas the thyroid has slower activity, but longer-lasting effects. Cannon (1927) noted that exposure to cold caused an increase in the rate of the denervated heart. It has also been reported that the serum taken from an animal exposed to cold raised metabolism of a second animal, into which it was injected. If the first animal had been thyroidectomized, the effect upon the metabolism of the second animal was not observed. Rats

exposed to low temperatures over a period of weeks showed thyroid hyperplasia and a rise in metabolic rate of as much as sixteen per cent. Thyroidectomized rats, however, showed no such rise in metabolism under similar conditions.

BODY TEMPERATURE AND SALT AND WATER METABOLISM.

Because of its high specific heat, water is capable of absorbing large quantities of heat, thus preventing high temperature rises in the cells. Those tissues in which heat is produced are high in water. Having absorbed heat from its source of production, water, because of its fluid nature, is capable of distributing heat equally throughout the body and carrying the excess to the surface, where it may be given off. Water thus acts as a buffer in high temperature changes, and as a vehicle of heat within the animal body; so water and its distribution are very important in the control of body temperature.

The water and salt metabolism and the blood chemistry are geared to a certain level of body temperature. Acidosis may occur in fever, but its occurrence is probably not as frequent as has been supposed. Low carbon dioxide tension in blood and alveolar air is usual during fever; but Koehler and others have found

decreased hydrogen ion concentration and consider the low bicarbonate to be compensatory to an alkalosis resulting from hyperpnea. Bazett and Haldane report similar findings following immersion of the experimental animals in hot baths. The ketonuria which often occurs in febrile conditions is an indication of fat metabolism, but is not to be considered as evidence of acidosis. No generalization as to the occurrence of acidosis or alkalosis can be made. The degree of hyperpnea, the presence of complicating renal and circulatory impairment, and the frequently associated inanition are factors which contribute to the ultimate acid-base balance in a given case.

The chloride level, normally very stable, is abnormally low in fever (Peabody, 1912). There is hemoconcentration and a loss of water into the tissues during fever; a salt retention is also found with this water retention in the tissues, thus establishing a viscious cycle. Barbour (1925) and his associates have shown that antipyretic drugs bring about dilution of the blood, which favors heat dissipation by radiation.

EFFECT OF BODY TEMPERATURE ON METABOLISM.

Due to its effects on muscle contraction, the most potent influence of metabolic increase is low environmental temperature (Hardy, 1940). Heat production

may be increased as much as twelve times normal by a cold bath at forty degrees Fahrenheit. Increased heat production lasts about ten minutes, then becomes depressed, and body temperature falls (Du Bois, 1937), when metabolism fails to keep up with heat dissipation. There is then a slowing down of the chemical processes, in accordance with van't Hoff's rule.

Metabolism is geared to a definite body temperature, and to change the temperature dissipation and resultant body heat causes a corresponding change in the chemical reaction. The higher the body temperature, the faster the rate of metabolism, which causes more heat and raises the reaction rate still more; and so the cycle goes, according to the van't Hoff principle regarding chemical reactions. For each rise of one degree Fahrenheit, there is a corresponding rise of seven per cent in metabolism. Thus, at a temperature of one-hundred-five degrees Fahrenheit, the basal metabolism would rise fifty per cent above normal (DuBois, 1936).

During these febrile states, katabolism also occurs, and protein is destroyed, as determined by the urea, creatinine, purines, sulfur, and phosphatase in the urine. Best and Taylor (1943) say that three hundred to four hundred grams of protein may be destroyed

daily. This is the state of affairs in all acute infectious fevers and is due to increased destruction and decreased production of proteins. Therefore, high carbohydrate intake and adequate proteins are imperative in proper treatment of acute infectious fevers. For this reason, we "feed a fever".

Woodyatt, Balcar, and Sansun (1919) found that during the course of continued intravenous injections of glucose in dogs and man, fever was observed under certain conditions--namely, when the rate of sugar injection was sufficiently in excess of the tolerance limit to produce a marked glucosuria with its concomitant diuresis, when the rate of water administration was less than the rate of diuresis, and when these conditions were sustained until the animal or man had lost a certain weight by dehydration. Chills were also observed to occur under the same conditions after the body temperature had begun to rise. Both chills and fever were seen to subside when enough additional water was administered. They concluded that after a sufficient quantity of water had been abstracted from the body, there was not enough left to sustain the normal processes of cooling by evaporation through the lungs and skin, and that the animals and man suffered a true thirst fever produced in this unusual way. It also might be added

that the extra concentration of sugar in the blood would extract water from the tissues. It is a common thought and experience among pediatricians that salt fever can easily be produced in babies.

## II

## Normal Temperature, with its Variations

### THE AVERAGE NORMAL TEMPERATURE.

Although 98.6 degrees Fahrenheit has been arbitrarily set as the normal, authorities are not in agreement as to the average normal. For practical and clinical purposes, that level is satisfactory; but, more correctly considered, it is near the upper limit of the average normal range. Then, too, this figure of 98.6 degrees Fahrenheit should be qualified as to the time of day in which the temperature was taken, remembering that this is a spot temperature and is sublingual, the rectal temperature usually being considered as one degree Fahrenheit higher. Brenneman (1943) objects to the usage of rectal temperature as one degree Fahrenheit higher than normal, stating that, in reality, the rectal is often the more correct of the two, as well as more stable, and should be the standard to which the oral temperature is subordinated. It is common usage, however, to imply

that the temperature is oral unless otherwise described, and for that reason, that usage will be followed throughout this thesis. The axillary temperature, when used, is one degree Fahrenheit lower than the oral temperature clinically.

Reimann (1935) says it is misleading to fix one figure, such as 98.6 degrees Fahrenheit, as the normal temperature. He found, by investigation of the oral temperatures in groups of apparently healthy people, that there is a fairly wide range of variation. Statistical analysis of some of these data showed the standard deviation of normal oral temperatures to be approximately 0.47 degrees Fahrenheit. On the basis of this standard deviation, it was predicted, by the use of statistical methods, that the average normal oral temperature in a large population would range from as low as ninety-seven degrees Fahrenheit to as high as 100.4 degrees Fahrenheit (fig. 2). He further states that in adults the average oral temperature can be placed at approximately 98.4 degrees Fahrenheit. In clinical practice, ninety-nine degrees Fahrenheit or above is abnormal. In persons confined to bed the average reading is somewhat lower, or about ninety-eight degrees Fahrenheit, while a temperature of 98.6 would be indicative of fever. These temperatures are correct, notwithstanding the

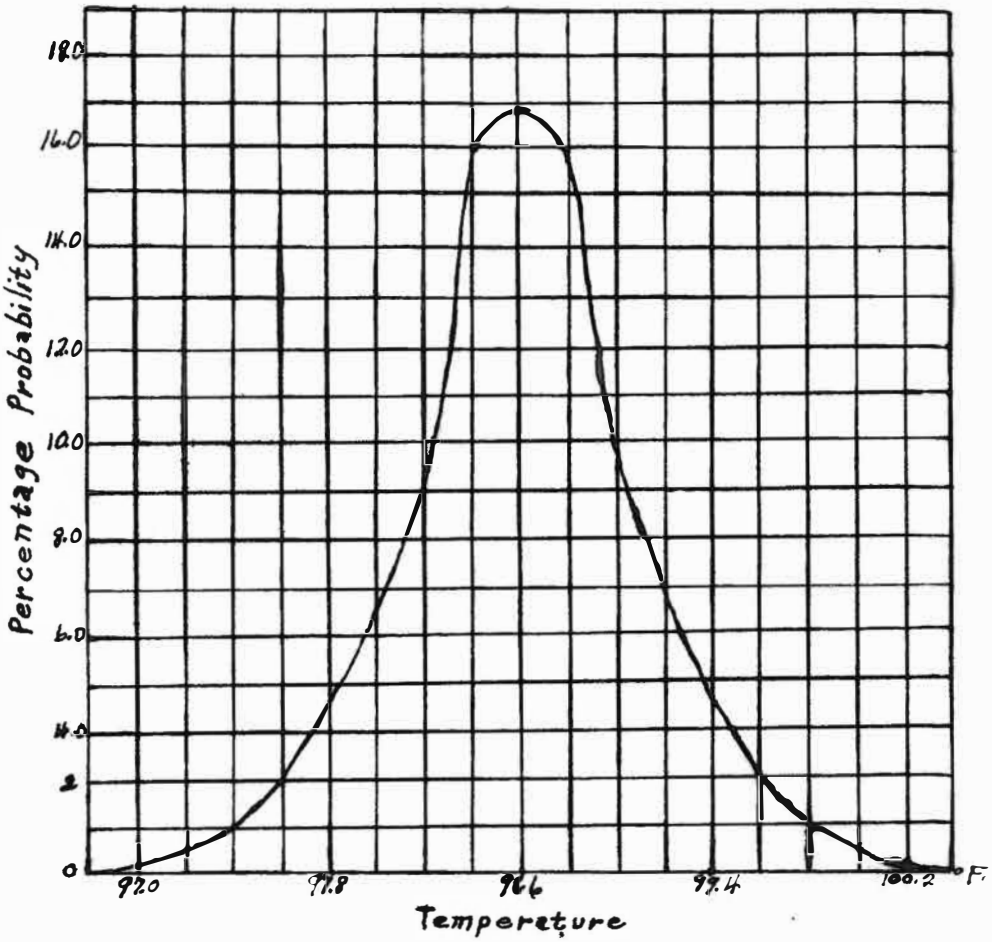


Fig. 2. Curve of the probable incidence of average normal oral temperature, constructed from a table prepared by Dr. Frances Vanzant. (Reimann, 1940).

errors in technique used in obtaining them, which are common and remarkable, particularly so of the oral and axillary, and leastwise of the rectal methods.

Neymann and Osborn (1934), in order to ascertain the exact temperature of viscera and subcutaneous tissue, constructed thermocouples and soldered them into spinal puncture needles. They found, by insertion of

these needles, that the depths were two degrees Fahrenheit warmer than the subcutaneous tissue of the thorax and abdomen. They also observed that there was gradual reduction in temperature as the thermocouples were inserted more distal, i. e., the subcutaneous tissue of the ankle is one degree Fahrenheit colder than the gluteal region. According to Reimann (1935) the skin of the hands and feet may have a temperature from five degrees to as much as twenty degrees below the oral reading. Neymann (1934) also found the temperature of the brain to be about one-half degree higher than the oral reading.

DIURNAL RHYTHM.

Homoiothermic though he may be, man normally runs a definite, rhythmical, twenty-four-hour cyclical temperature with a diurnal rhythm. The highest temperature occurs between four and six o'clock in the afternoon, gradually tapering down to the low, which occurs about four o'clock in the morning, or just before awakening from sleep. Best and Taylor (1943) give this variation of about five-tenths to one degree Fahrenheit, the maximum occurring in the late afternoon or early evening, and the low occurring about four or five o'clock in the morning. The times of maximum and minimum temperature

might be reversed in night workers, but not completely so. In infants, we find this diurnal variation absent for the first few months of life, and this has caused somewhat of a problem in determining the basis for their daily body temperature rhythm. It is supposed, however, that the heat-regulating mechanisms are not fully developed at birth, because, within a few months, the diurnal rhythm begins to appear.

Kleitman, Titelbaum, and Hoffman (1937) studied one hundred cases at Chicago Lying-In Hospital and at Bob Roberts Memorial Hospital. They compiled records of four to ten children in each of the following age groups: newborn, six months, seven to twelve months, thirteen to twenty-four months, two to six years, and seven to thirteen years. These men demonstrated the fact that there may be a diurnal variation of newborn babies. They made no positive statements or conclusions, however; and I might add that the variation of the daily routine as compared to the more quiet and less noisy night routine was not considered in this study. These workers also mentioned a brain tumor case in which there was no diurnal variation, as well as a hydrocephalic which did show a diurnal change. The importance of daylight and daily routine in regard to

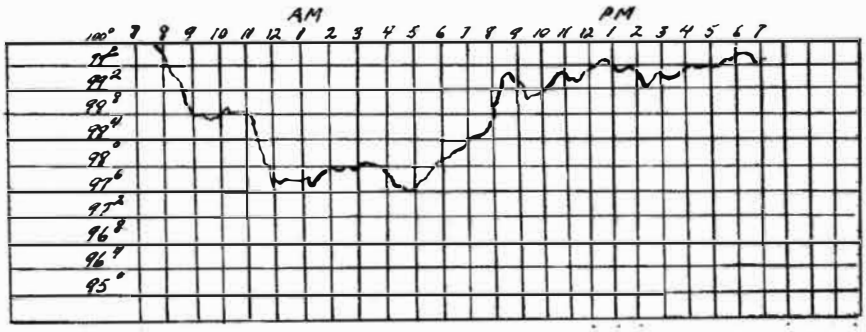


Fig. 3. Fluctuations in body temperature of G. W. H. during a "normal" day. (Benedict, 1904).

complete relaxation might be questioned (fig. 3 and fig. 4). They concluded, further, that while there may be a diurnal variation in young infants, the diurnal cycle, in the sense of a regularly recurring and superimposable

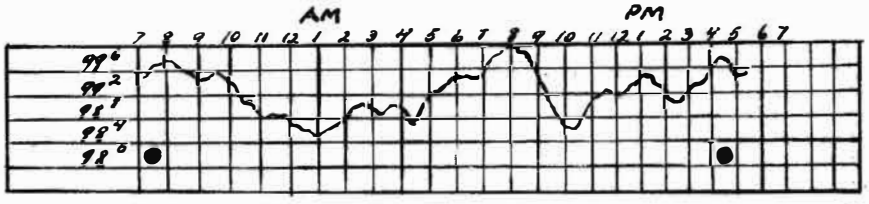


Fig. 4. Fluctuations in body temperature of G. W. H. on the tenth day of inversion of the daily routine (night work). (Benedict, 1904).

variation, first appears during the second year of the child's life. A gradual approach to that state can be discerned during the first year. Burton (1939) found that several observed cases were without diurnal rhythm until they were two years of age.

Although diurnal rhythm is affected by daily

routine, it must be admitted that there are other factors, since reversal of the routine does not completely reverse the curves of the daily changes. However, Benedict also reports complete reversal of the daily temperature rhythm changes of birds with nocturnal habits; so perhaps the factor of growth and maturation has some permanent effect on temperature regulation.

Van der Bogert and Moravec (1937) studied the temperatures of more than seven hundred healthy children and noted oral temperatures above 98.6 degrees in over forty-three per cent at the ages of seven to eight years. In the group between thirteen and fifteen years, only eight per cent had temperatures higher than 98.6 degrees Fahrenheit. He concluded that stability of temperature did not occur until about puberty (fig. 5).

It is a well known fact that rectal temperature runs about a degree higher than oral temperature, and also that the body temperature rises several degrees with exercise, the elevation varying directly with the intensity of the exertion. It is not widely known, however, that exercise will cause a rise in rectal temperature of several degrees, while the oral temperature taken at the same time may remain unchanged, may rise slightly, or may even drop. Brennemann (1943) performed a number of experiments with children, using various

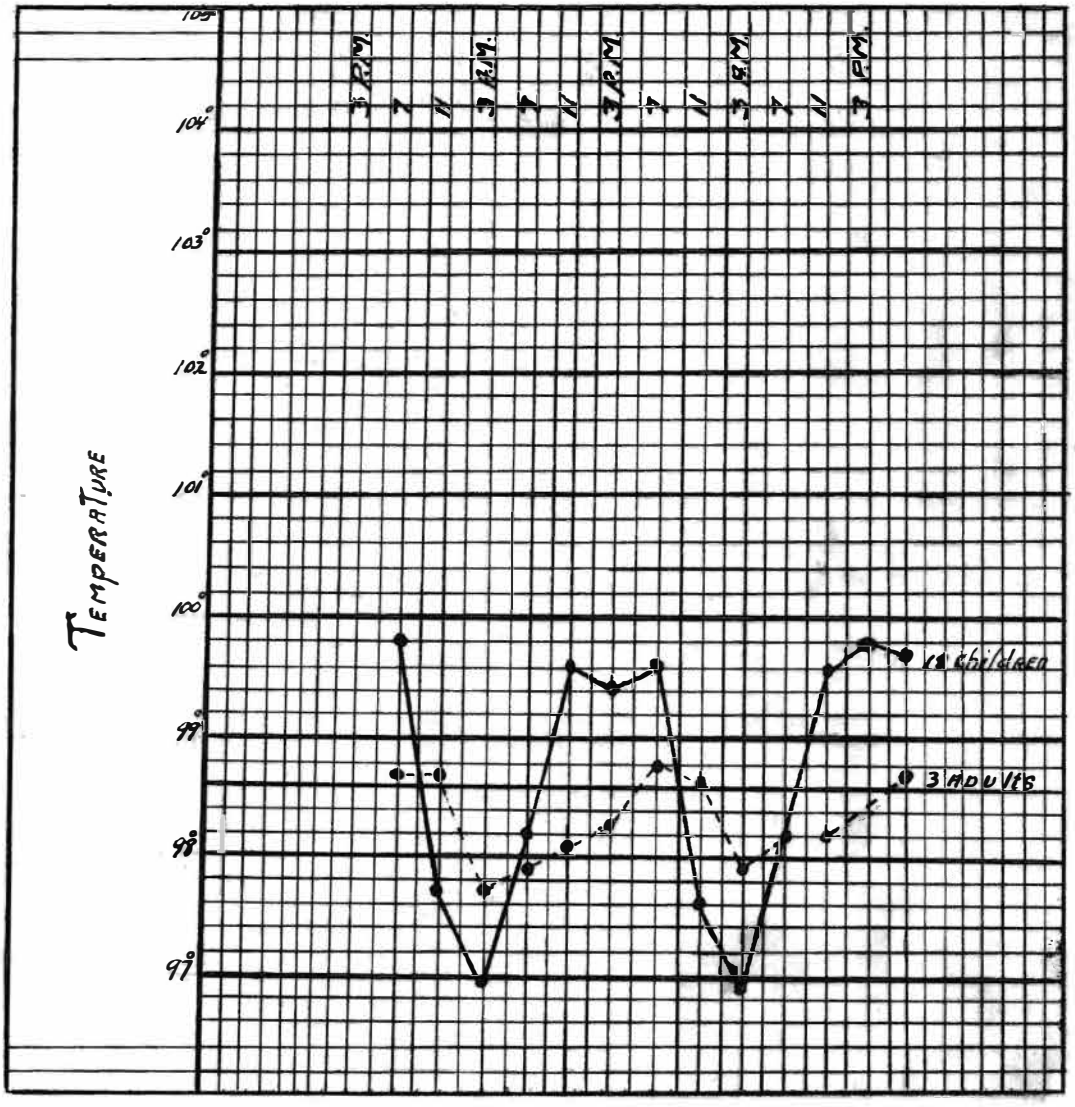


Fig. 5. Comparative chart of the temperature variations of children and adults. (Van der Bogert and Moravec, 1937).

amounts of exercise, and obtained quite conclusive results to that effect. Oral temperatures in these cases varied only slightly and were unpredictable, whereas the rectal temperatures raised from one to four degrees Fahrenheit and returned to normal in about thirty

minutes. He also wrote of a tuberculous patient with calcified hilar nodes, who had a normal oral temperature.

TEMPERATURE CHANGES WITH THE MENSTRUAL CYCLE.

In 1904, van de Velde discussed the variations in body temperature during phases of the menstrual cycle. Since that time, at least a score of papers have been written on this subject, particular emphasis being placed on the correlation of temperature changes and ovulation. Morris and Greulich (1941) made a convincing clinical test of the accuracy of temperature records as an indication of ovulation. Laparotomies were performed on fourteen patients, whose temperature records were available. In eight cases ovulation was expected; in six cases it was not. Inspection of the ovaries at laparotomy confirmed the prediction in every case.

Tompkins (1944), of Philadelphia, discussed a series of cases and presented typical graphs, together with details of the variations of the temperature curve for the entire menstrual cycle. The temperature is relatively low during the first part of the month, drops to a minimum about the time that ovulation occurs (fig. 6), and rises definitely thereafter to a relatively

high level, which is maintained until the next menses, at which time the temperature drops abruptly. After

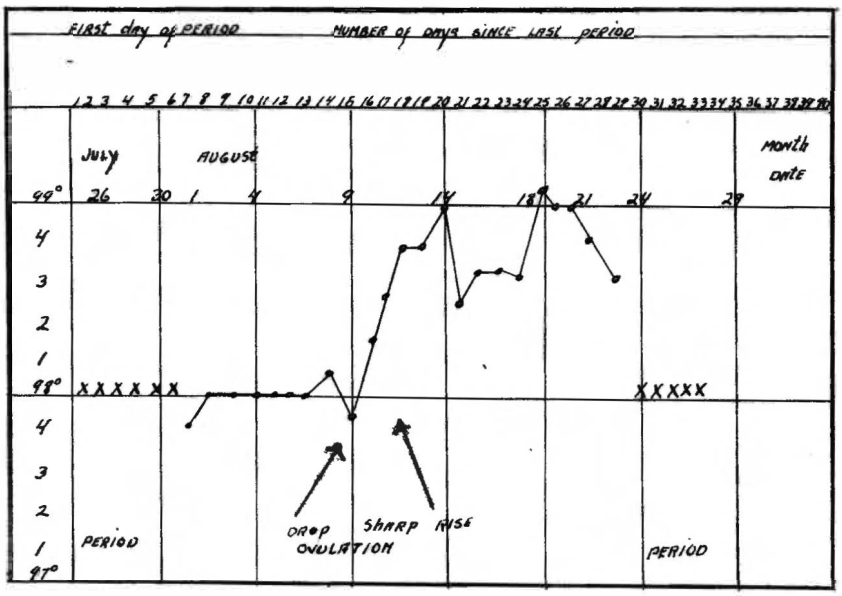


Fig. 6. An ideal temperature graph submitted by a patient. Note (1) the relatively low temperature prior to ovulation, (2) the slight drop on August 9, which occurs at ovulation, (3) the sharp rise following ovulation, (4) the relatively high level after ovulation, and (5) the sharp drop when menstruation begins. The temperatures shown are exactly those submitted by the patient but have been regraphed and annotated for publication. (Tompkins, 1944).

fruitful insemination, the temperature is sustained at a relatively high level (fig. 7). It might be added that here again the total variation is approximately a degree and that this variation is calculated from the normal, under standard conditions, and at the same time

before rising in the morning. Before the menarche, after the menopause, and in men these temperature fluctuations are not present.

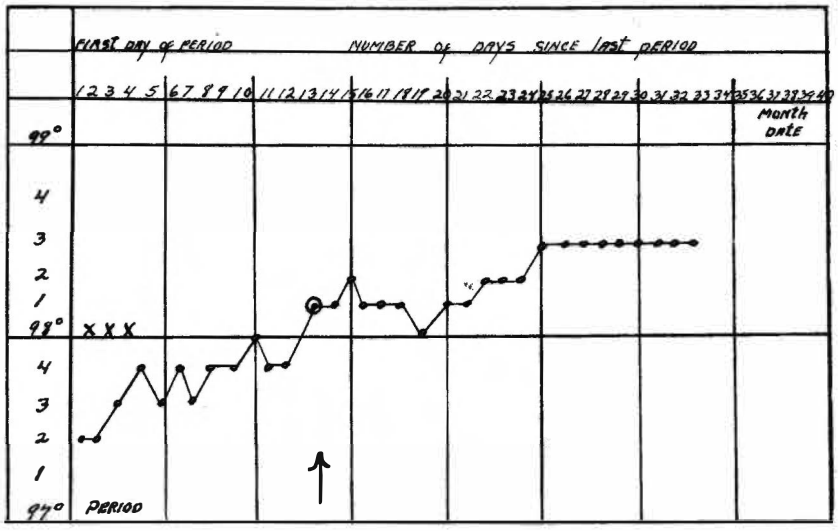


Fig. 7. Successful artificial insemination timed by the graphic method. Periods very regular, twenty-eight to thirty days. Artificial insemination had been unsuccessfully attempted on two previous occasions on the 14th day before the expected period. As the graph shows, fruitful insemination (arrow) occurred fifteen to seventeen days before the period was due. Note the sustained elevation of temperature, which is typical of early pregnancy. Pregnancy has progressed to the fifth month uneventfully. (Tompkins, 1944).

Rubinstein (1938) estimated the ovarian activity by the consecutive daily study of basal body temperature and basal metabolic rate and found that rectal temperatures reached a low level during menstruation, with a lower level three days later, and the lowest

level around the tenth day. Endometrial smears correlated ovulation with the period of lowest temperature.

## III

## Abnormalities of Body Temperature

### HYPOTHERMIA.

Hypothermia is restricted to a state in which the average bodily temperature is significantly below normal. It is less common than other aberrant conditions of body temperature.

Reimann (1935) checked a number of cases of hypothermia and eliminated those with myxedema, Addison's disease, cachexia, or shock, those convalescent from infections, and those with chronic conditions known to cause or to be accompanied by hypothermia. It was remarkable that his selections of nine patients with hypothermia were all men with predominant signs of vagotonia, whereas in another article on hyperthermia, the cases were predominantly women. However, consistent differences in the temperatures of men and women are meager. As the studies progressed, it became more and more evident that the patients selected for observation had most, if not all, of the signs and symptoms characteristic of "neurocirculatory asthenia", also called

"soldier's heart" and "effort syndrome". Had these cases been encountered during wartime, most of them, no doubt, would have been classed as such. Since neuro-circulatory asthenia is a serious problem in all wars, it was found to be of immediate importance in this war and was one of the frequent causes of invalidism among both soldiers and civilians (Lewis, 1940). The nine patients studied here had a consistently low temperature level from 96.4 degrees Fahrenheit to ninety-eight degrees Fahrenheit. Besides the hypothermia they usually had the other signs of vagotonia, such as hypotension, bradycardia, palpitation, sweating, low basal metabolic rates, and numerous bizarre complaints for which no organic basis could be found. Some of their complaints were constipation, dry mouth, and dilated pupils, characteristic of sympathicotonia. One case had a tachicardia. The most consistent statement to be made about these cases is that all displayed evidence of nervous instability and imbalance; it should also be recognized that needless surgery and expensive, investigative procedures might be prevented. Subnormal temperatures of local areas frequently occur due to poor circulation, such as in the feet of severely arteriosclerotic diabetics, or by tourniquets, preventing good blood supply, whereas generalized subnormal temperatures are rare.

HYPERTHERMIA.

Hyperthermia is a state of the body in which there is an elevation of body temperature above the normal. It may be of various origins.

From the beginning of medicine, Hippocrates, Celsus, Sydenham, and many others considered hyperthermia to be important as a defensive mechanism against disease, "vis medicatrix natural". But early in the nineteenth century Claude Bernard and Liebermeister regarded fever as deleterious, largely because of the development of cellular pathology by Virchow. Since then, Naunyn and others have shown the pathology to be due to micro-organisms, rather than to the fever, with the exception of extremely high fevers of long duration.

The etiology of hyperthermia is variable, but there are three theories put forth by Cramer (1926) as to the genesis of fever. These postulations are, as follows:

1. Abnormal distribution of body water with hemoconcentration. It is disputed whether or not this is the cause of or the effect of fever.
2. Over-function of the thyroid and adrenal glands.
3. Stimulation of the hypothalamic centers.

To me, these theories might well be linked together in

one complex and necessarily related etiological process in the production of fever.

As for the first theory pointed out by Cramer, Reimann (1932) noted a change in the suspension stability of the blood. Fever and this suspension instability may occur separately, but they usually occur together. There is a globulin and fibrinogen increase in the blood. These plasma protein changes are thought to aid in the agglutination of bacteria.

Jung (1935) observed a definite increase in the leucocyte count during hyperthermia. There is an increased blood volume, which is attributed to two factors: (1) contraction of the spleen, discharging blood rich in cells into active circulation, and (2) dilution of the blood by passage of water from the tissues to the blood stream.

Hemoconcentration, as determined by plasma protein, red cell count, and blood viscosity, is found in cold environments. There seems to be a moderate loss of water from the blood, chiefly to the tissues. The exact mechanism of this loss of water to the tissues is not well known, but Barbour and Hamilton (1925) have shown that cold, applied locally after section of the splanchnic nerves, causes anhydremia by transudation of water

into the skin and cooled area. They conclude that the migration of water is due to the constriction of the cutaneous arterioles and to the consequent slowing of the blood flow in the capillary. Anoxia of the vessel wall is the result, increasing the permeability of that membrane. Thus, there are central nervous system effects causing vasoconstriction and peripheral effects, due to anoxia, causing increased permeability, both of which result in hemoconcentration. It might be added that the cold may cause direct injury to the vessel wall, thus producing increased permeability; nevertheless, blood studies are very similar. Barbour and Hamilton (1925) also found that animals in which the cord was injured or divided in the upper thoracic region did not respond to the cold bath as did the normal animal, and that there was no concentration of blood without the central effects.

Sheard (1935), in a symposium at a Mayo staff meeting, stated that leucocytes travel four times faster at ninety-five degrees Fahrenheit than at seventy-seven degrees Fahrenheit. As the temperature of the body is elevated above normal, the physical properties of the leucocytes change from the gel toward the sal state, thereby becoming more permeable and better able to ingest greater numbers of bacteria or other foreign bodies.

Fever accompanying infection exerts an adverse influence on the growth of bacteria, favors phagocytosis, diminishes the potency of toxins, and stimulates the development of antibodies. Sheard also observed that the pulse rate rises and that ninety-four degrees Fahrenheit is the temperature of maximum perspiration.

Hyperthermia may be classified as follows:

1. Physical hyperthermia.
2. Climatic hyperthermia.
3. Hyperthermia due to superimposed exercise.
4. Hyperthermia due to superimposed humidity.
5. Heat stroke.
6. Neurogenic hyperthermia.
7. Spurious hyperthermia.
8. Dehydration hyperthermia.
9. Chemical hyperthermia.
10. Septic hyperthermia.
11. Infectious hyperthermia.

Physical hyperthermia results from a hot environment, in which heat elimination is unable to cope with the situation. This condition occurs as an industrial problem and is clinically important, since the mere administration of sodium chloride and water will prevent the development of shock.

Climatic hyperthermia occurs in a hot, humid climate, which prevents proper heat elimination. High environmental temperatures and solar radiation do not necessarily cause a hyperthermia unless the heat elimination is deficient.

Superimposed exercise causes hyperthermia in relation to severity of the exercise and the duration of the exercise. A previous experiment by Brenneman (1943) with children showed an increase in rectal temperature of from one to four degrees after vigorous exercise. Again, Searcy (1944), after checking a hyperthermic patient for undulant fever, typhoid, malaria, and similar diseases, discovered that when the patient discontinued the chewing of gum, the temperature became normal. Later a whole family troubled with fever became normal after the discontinuance of the habit of chewing gum. An experiment with twenty apparently normal nurses was performed, in which the oral temperature was taken every five minutes during one-half hour of gum chewing. There was an average rise of four-tenths degrees Fahrenheit, and the highest rise was 1.2 degrees Fahrenheit. The temperatures all returned to normal within ten minutes after the chewing ceased. Searcy concluded that the hyperthermia was purely physiological and varied with the

vigor of the gum-chewing. There is no other literature on gum chewing hyperthermia, but it is conceivable to me after observing the vim and vigor with which some people chew their gum.

Humidity may cause hyperthermia, in that it interferes with one of the major mechanisms of heat dissipation, that of vaporization of water from the body surface. All of these previous types of hyperthermia are temporary, lasting as long as the external environmental condition exists. Once the environment is corrected, the body temperature will correct itself, returning to its normal homoiothermic level in a matter of about ten to fifteen minutes, and will remain normal so long as the environment is within the normal compensatory limits of the heat-regulating factors.

Heat stroke is a combination of the above conditions, in which the heat mechanism is disturbed and which results in a definite pathological syndrome. Even after the environmental temperature has been corrected, pathological symptoms and findings may be observed for hours, or days, or longer. In heat stroke there is prostration and an absence of sweating, the mechanism of which is disturbed by the abnormal condition. Osler quoted F.A. Packard on thirty-one patients with heat stroke, who were admitted to the Pennsylvania Hospital in 1887. The

majority of their temperatures were between one-hundred-ten and one-hundred-eleven degrees Fahrenheit (MacNeal, 1939).

Neurogenic hyperthermia is a term used indiscriminately when there is disease of the central nervous system with fever. With this condition, there is a typical syndrome of a rapid rise of rectal temperature, relative warmth of the trunk, and icy dryness of the skin of the extremities, venous blotching often appearing in nondependent portions of the skin of the extremities and less frequently in the trunk. Pilo-erection may be present, together with anhydrosis. Thus, heat loss is obviously reduced to a minimum. The patient is quiet, rarely agitated, and usually unconscious. Hyperpnea is often present, with the respiratory rate as high as forty or fifty per minute. The blood pressure may be low, even with the extreme tachycardia.

The above syndrome of neurogenic hyperthermia is frequently observed following operative procedures on the pituitary fossa, the region of the third ventricle, or the posterior fossa, as well as after head injuries. The temperature rise usually occurs after general anesthesia wears off, or at least within the first twelve hours after an operation or head injury.

The height of the fever may vary, and it would go over one-hundred-five degrees Fahrenheit but for good nursing. The height of the temperature is no indication of the severity of the injury, nor is it a prognostic until the fever is in the subsiding phase.

Twenty autopsy specimens from patients with neurogenic hyperthermia were studied. In sixteen of these, there were definite gross lesions in the hypothalamus or the brain stem, where they could involve experimentally demonstrated heat-regulatory centers or pathways. Patients may have edema or small hemorrhages in these areas, thus causing the typical neurogenic hyperthermia. Prophylactic measures are genuinely effective in lowering the incidence and mortality of these cases.

Woodhall (1936), in a study of acute cerebral injuries, found that about seventy to seventy-five per cent of these cases would, after an early drop or after starting from a normal level, show a mild hyperpyrexia to one-hundred-one degrees rectally, and a slow, regular decline to normal within from twenty-four to thirty-six hours. The next group, with a more severe injury and unconsciousness over a longer period of time and with initial bradycardia, would have a persistent, moderate rise in temperature. This latter group had an extradural hematoma. His third group was composed of

cases with a still more severe type of injury, in which the temperature was high and unremitting. These patients had a relative bradycardia and Cheyne Stokes type of respiration.

Over a period of several years, persons without obvious infection or organic disease, whose average temperature was slightly, but continuously, higher than the usually accepted normal, were selected for special study (Reimann, 1940). Of twenty persons studied, seventeen were women. Most of these cases had been suspected for months or years of having some obscure, underlying infection or other disease to account for the "fever", and many had been subjected to needless prolonged, expensive investigations or treatments in an attempt to discover the cause. Because of the elevated temperature, the condition was at first regarded as habitual hyperthermia; but it soon became evident that in most cases the "fever" was only one factor among many others which occur in certain so-called neurotic persons. Furthermore, most of the neurotic patients had signs and symptoms of syndromes, commonly known as sympathicotonia or vagotonia, chiefly the former, or a combination of the two. It was also pointed out that average body temperature may vary among different normal persons, just as does the pulse rate or blood pressure, and deviations

from the accepted standard of the norm need not always be looked at as evidence of disease. Nevertheless, a person whose average oral temperature is higher or lower than 98.6 degrees Fahrenheit and who has the symptoms of a neurosis, of whatever nature, can hardly be regarded as normal.

Spurious hyperthermia is a state of hyperthermia in which no organic basis can be found. These fevers may be irregular, and they do not coincide with other physical findings of such patients. Nevertheless, infections and other physiological disturbances cannot be unraveled in the long line of laboratory routine used.

MacNeal (1939) reports several cases of hysterical fever. One of the cases was a woman who, after a serious disappointment on Sunday morning, fell into a narcoleptic state and was absolutely insensible. The following night her temperatures, axillary and vaginal, reached 111.2 degrees Fahrenheit. On Monday and Tuesday the temperatures reached the same high level. The patient recovered on the fifth day after the condition appeared. Deception seems to have been reliably excluded in this case. Since the details of the conditions are not given, we cannot state the physical status of these patients. It is of value, however, to know that high

temperatures do occur and should be checked. MacNeal concludes that a body temperature of approximately 114.8 degrees is the physiological maximum with which life is compatible.

Richet, cited by MacNeal (1939), in his monograph on animal temperature, tabulated one-hundred-nine cases of hyperthermia in man with temperatures ranging from 107.6 to 112.2 degrees Fahrenheit. There were thirteen survivals of this group. He rejected as unreliable several reported observations of temperatures from 111.4 to 122.0 degrees Fahrenheit with recovery, and expressed unwillingness to accept as valid any observation of temperature above 114.8 degrees Fahrenheit. This decision was based not merely upon clinical studies, but also on extensive physiological experimentation and observations on various mammals. MacNeal agrees with Richet and mentions the famous cases of Heber Jones (1891), as well as the patient of Du Castel (1884), who, by tapping the upper end of the thermometer, succeeded in registering a maximum temperature of 111.6 degrees Fahrenheit, with recovery.

Classic cases of trickery are worthy of mention. Little (1880) reported two cases with temperatures of one-hundred-twelve to one-hundred-twenty-five degrees

Fahrenheit, which were repeated with two thermometers after several days of high readings. The two thermometers simultaneously used in the same patient recorded a great variation, and fraudulent temperature was detected, which the patient admitted having produced by means of poultices and hot water bottles.

Galbraith reported a fraudulent case in Omaha, in 1891, in which axillary and oral temperatures of one-hundred-thirty-seven and one-hundred-thirty-one degrees Fahrenheit respectively were simultaneously observed in a nude girl, sitting on a chair. Half an hour later the temperature was normal, and the fraudulence was proven; but the technique used was never discussed.

Another case of a contortionist (Jones, 1891) produced repeated temperatures of one-hundred-eight to one-hundred-fifty-six degrees Fahrenheit. This was also proven to be spurious. Many other similar cases have been reported, which were produced by the use of hot objects, by swinging the thermometer opposite to shaking the mercury down, and by tapping the end of the thermometer.

Schnur (1940) wrote up four cases of women with fever, of fraudulent origin, which they used as a means of escape from an intolerable environment and as a method of gaining attention. These cases were

diagnosed, after a long period of reported fever, by the disparity between the reported temperature and the bradycardia and normal blood counts, as well as by the fact that the patients looked well.

Checks used against fraudulent fevers are also numerous; most important of these is close observation. Other checks are the simultaneous use of two thermometers in various locations, and, in extreme cases, a check on the temperature of fresh urine.

Because water is so important in the transportation of heat to the surface and then in the liberation of heat from the surface, excess water loss from the body by any other route would decrease the heat dissipation efficiency. Also, a decreased fluid intake with a normal water output will cause decreased body fluids and will result in fever. Again, a relative increase in the salt concentration not only will hold the water in the tissues, thus preventing water loss, but also will hinder circulation, further decreasing temperature balance efficiency.

Salt and lactose are hydropigenous substances, causing water retention. The salt and lactose molecules have an affinity for water. Salt draws water into the tissue cells, while lactose draws water into the

blood stream. It is then eliminated by the kidneys, as in diabetes mellitus, and thus prevents normal dissipation, resulting in anhydremia and fever.

The posterior pituitary gland secretes a pressor principle, previously discussed under the glandular attributes to or against fever. Tumors of the gland or atrophy may cause diminution of the pressor principle, resulting in excess water loss from the kidney, as in diabetes insipidus, and thus causing fever.

A common cause of fever in newborns is the normal water loss by evaporation and urine without an adequate fluid intake (Leebron, 1938). This frequently occurs before the mother's milk starts, and sometimes fluids are neglected the first few days with formula-fed babies.

Many simple chemical substances cause fever on subcutaneous injection. These substances are absorbed into the blood stream, where they can contact the vital hypothalamic centers very quickly. They include plain water, salt solution, and proteins and their split products, and probably act by causing a break-down of tissues. A considerable number of drugs, among them caffeine, cocaine, methylene blue, and many others, are also fever-producing agents when injected in this manner.

The observation of Gregg (1935) that hypotonic solutions of sodium chloride increase heat production and produce hyperglycemia in dogs may be of significance in this connection. Unless, as apparently happens in mature animals and adult humans, this is compensated by increased heat dissipation, a rise in temperature is unavoidable. Caffeine and cocaine act as pyretics, either when injected or when applied to the basal ganglia.

MacNeal states that one of the most constant and striking features characteristic of hyperthermia is the invasion by and growth of pathogenic organisms. Break-down products of bacterial proteins or parasites, as well as toxins liberated by some organisms, act upon the heat regulating center, altering the thermostatic level at which body temperature is maintained. They do not act by weakening or paralyzing the heat regulatory centers. According to most investigators, the nature of the processes is identical in most infective diseases (Du Bois, 1935).

The initial change is not due to greater heat production, but rather to a disturbance in the mechanism for the regulation of heat dissipation. Decreased elimination leads to a temperature rise, which, as

previously shown, causes further increase of metabolism.

In most fevers the body temperature shows sudden elevations and depressions. In the second week of certain infections, such as pneumonia or typhoid fever, the body is maintained at an elevated temperature, with fluctuations that are scarcely greater than those found in health.

The sudden rise and fall are best illustrated in malaria fever and are similar to the sudden changes of temperature with intravenous injection of foreign protein. The coldness, pallor, and chills are caused by decreased blood flow through the skin, resulting in stimulation of cold receptors, which give the patient the sensation of coldness and result in the symptom of shivering (Wiggers, 1944).

No constant relation exists between the severity of the infection and the height of the fever (Hewlett, 1928). It is well known, however, that in mild infections the temperature response is usually mild. If the patient is already weak and debilitated, the temperature response to infection is not normal and may be extreme. The marked fluctuation and periodicity of fever is not well understood. In some, this seems to be an exaggeration of the normal diurnal variation, particularly in tuberculosis and in the declining stages of

typhoid fever. It may possibly depend on the factors that produce normal diurnal variation. At any rate, the fluctuation is greater after eating of food, exercise, and other activities of the day.

Malaria has a periodicity, but not a daily fluctuation. It occurs with sporulation, starting first with a chill.

The pyrogenic factor, according to Menkin (1945), seems to be a proteolytic split product, brought about by the action of necrosin, which, in turn, either is an enzyme or, in its present state of purification, displays enzymatic activity. Purified necrosin, as such, is nonpyrogenic. This fever-producing substance is associated with euglobin, a relatively insoluble fraction of exudative material, except in the presence of sulfate ions; it is also soluble in isotonic saline. This material results from the chemical derangement of the cell in the presence of inflammations and is termed pyrexin. Its mode of action may be by direct effect on the heat-regulating centers of the hypothalamic region. This pyrogenic substance, pyrexin, is nondiffusible and heat stable. It is not present in normal blood, but is present in blood with hemolyzed cells.

Blood or foreign proteins in the peritoneum will

cause a rise in temperature. Dill and Isenhour found fever in fifty-eight to ninety-one per cent of patients with bleeding peptic ulcers.

Chief cause of fever and chill after venoclysis lies in the presence of substances derived from the metabolism of chromogenic bacteria, which are found abundantly in river water. These substances are extremely resistant to heat and cannot be broken down by routine distillation processes. They can be broken down, however, by high pressure steam carried at sixty pounds in the main.

The critical temperature, beyond which life is impossible, varies somewhat with the individual. Clinically, about one-hundred-eight degrees Fahrenheit is the maximum, but complications are usually present in these cases.

Holbrook (1939) reports a case history of a patient who developed a rectal temperature of one-hundred-fifteen degrees Fahrenheit and who, on several occasions during the same period of illness, gave temperature readings in excess of one-hundred-ten degrees Fahrenheit, with ultimate recovery. Von Haam and Frost (1939) induced artificial fever in laboratory animals and studied changes produced in the parenchymatous organs. The

most frequent pathological change was of a vascular nature, namely, congestion and hemorrhage. Cytoplasmic changes and cellular necrosis were especially marked in animals which had suffered a temperature elevation of one-hundred-nine degrees Fahrenheit for a period of several hours, and were less frequently observed in animals which had died after a short exposure to rapid temperature rises. Those animals which survived repeated, short-lasting exposures to a temperature of 106.5 degrees Fahrenheit showed no parenchymatous necrosis or replacement fibrosis at autopsy examination. These findings indicate that time is a necessary factor in determining damage to body tissues from temperature elevations, and that fever over a brief period of time is not harmful to the cells of the body.

Smith and Fay (1940), after observing the relative infrequency of neoplasms in the extremities, tried lowering body temperature as a method of treatment for cases. Since the temperature of the extremities is around eighty-six to eighty-eight degrees Fahrenheit, they reasoned that a lower body temperature might be of value in cases of cancer of the torso. Following studies of the effect of cold locally upon cancerous tissue, it was felt that if it were possible to reduce

the entire body temperature to subcritical temperatures of eighty-five to ninety degrees Fahrenheit, it might be possible to find similar regressive cell changes in metastatic foci.

From December, 1938, to October, 1939, thirty-three patients were subjected to seventy-five inductions of generalized reduced body temperature, ranging from seventy-four degrees to ninety degrees Fahrenheit. All of these were hopeless terminal cases of cancer.

The general impression is that any prolonged reduction of temperature below ninety-four to ninety-five degrees Fahrenheit was inevitably fatal. These studies have brought out the fact that patients can be maintained for periods as long as five to eight days at temperature levels in the eighties.

Fatal cases of hyperthermia, according to Kopp (1938), may be explained on a basis of increased vascular permeability, leading to visceral congestion, cerebral edema, hemorrhagic encephalitis, and edema of the heart, lungs, and gastro-intestinal tract. These findings, according to Kopp, are typical of the so-called "shock syndrome". Death during or immediately following fever therapy treatment is due to vascular collapse (Hartman and Major, 1935).

# IV

## Conclusions

Body temperature control is so complicated in its ramifications that the control centers are dependent upon the physical condition of the individual, and vice versa. The factors of heat regulation are very sensitive.

The center of heat control is located in the hypothalamic region.

The central control of shivering is in the posterior portion of the hypothalamus and is stimulated by the sensation from a cool environment, at whatever level the threshold of body temperature might be.

Body temperature is not the same for all individuals, varying among different people; it also has a number of physiological variations in the same person. The temperature of 98.6 degrees Fahrenheit is not, technically speaking, the normal, but is, rather, the average for the group. One of the normal temperature changes is the diurnal variation, which is not established in children until about the second year of life and which remains unstable until puberty. Women have a definite temperature cycle corresponding to the menstrual cycle, in which ovulation occurs at about the low point of the

temperature cycle.

Hypothermia, which is relatively uncommon, is important as a sign of a vagotonic condition.

Hyperthermia may be of very complicated and indirect origin and may be classified as to its etiology.

There are a number of physiological changes in the body that occur with hyperthermia and that are indicated by a feverish state. When these conditions are corrected, the fever leaves; thus, fever is an indication of the state of the body, whether in health or disease.

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