FEVER

AND THE REGULATION OF BODY TEMPERATURE

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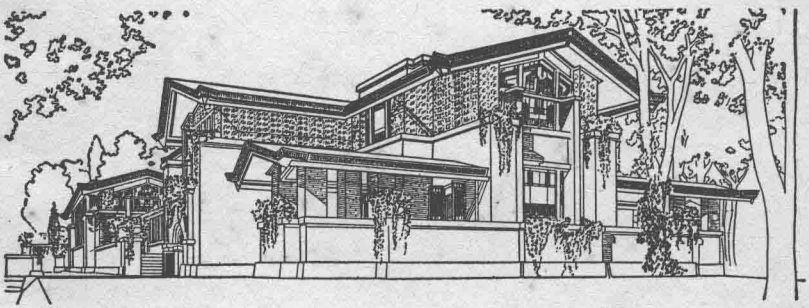

CHARLES C THOMAS • PUBLISHER
Springfield • Illinois • U.S.A.

CHARLES C THOMAS • PUBLISHER
BANNERSTONE HOUSE
301-327 East Lawrence Avenue, Springfield, Illinois

Published simultaneously in The British Commonwealth of Nations by
BLACKWELL SCIENTIFIC PUBLICATIONS, LTD.,
OXFORD, ENGLAND

Published simultaneously in Canada by
THE RYERSON PRESS, TORONTO

Printed in the United States of America

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Publication Number 13

AMERICAN LECTURE SERIES

A Monograph In

AMERICAN LECTURES IN PHYSIOLOGY

Edited by

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INTRODUCTION

FEVER, one of the most dramatic manifestations of disease, has been studied by physicians since the time of Hippocrates. It has been accepted as an aid in diagnosis and prognosis and has been fought as though it were both a disease and a symptom. It is so common that it seems simple and we take it for granted that sick people will develop fever. But why do they develop fever? Why don't normal people have fever? What is it that controls our temperature? How does the temperature change?

The Normal Body Temperature

At the very start it would be desirable to determine exactly the normal body temperature. We might state categorically that it is 37°C (98.6°F). This is merely a rough approximation, good enough for ordinary purposes but highly misleading in any scientific discussion. That pretty little arrow indicating normal temperature on the clinical therometer is deceptive and does more harm than good.

In the first place there is no *one* normal temperature but instead a fairly wide zone that shifts up and down with the time of day and with other factors. In the second place no one quite understands what we mean by "body temperature" and no one can measure the average temperature of the human body. Clinicians all realize that there is a difference of about one degree Fahrenheit between oral and rectal temperatures but forget that there are hundreds of other parts of the body with different temperatures. For example the skin and a large mass of subcutaneous tissue averages 2-4°C. cooler than the interior.

Normal or Normality

A. C. Ivy (1) of Chicago, has recently published an illuminating article entitled "What is Normal or Normality." As an illustration of his thesis he has used the measurements of the oral temperatures of 276 medical students seated in class between 8 and 9 A.M. and has plotted the results in Fig. 1. Treating the data statistically he has found the mean to be 98.1°F. and has drawn lines showing one standard deviation and two standard deviations (Figs. 1 and 2). About 68 per cent of the measurements were between 97.7°F. and

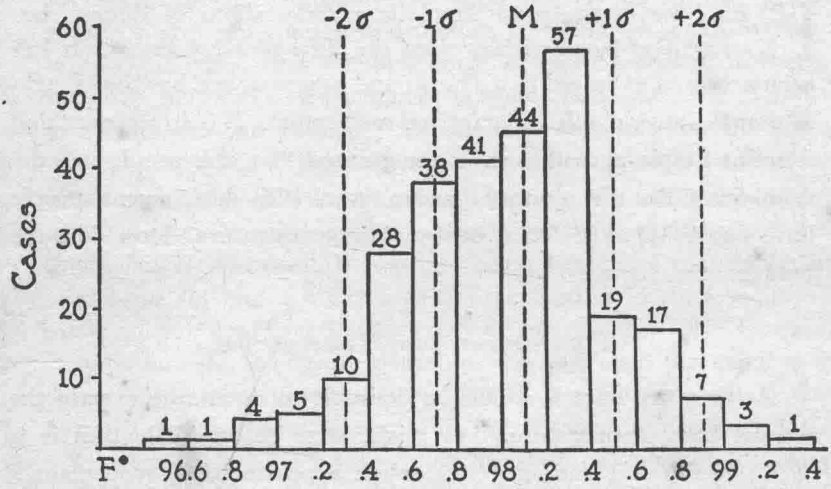

FIGURE 1

A. C. Ivy's record of oral temperatures in 276 medical students seated in class between 8 A.M. and 9 A.M. Mean 98.1°F. (36.73°C.); Standard Deviation (σ) plus/minus 0.4 degree F, the range 96.5 to 99.3 F. (From Quart. Bull. Northwestern Univ. Med. School.)

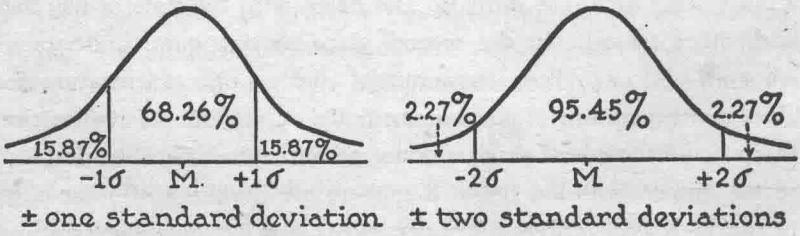

FIGURE 2

One and two standard deviations showing the distribution of readings in Ivy's graph. (Ibid.)

98.5°F. (36.6 - 36.9°C.), or within one standard deviation from the mean, and 95 per cent between 97.3°F. and 98.9°F. (36.3 - 37.2°C.). Ivy goes on to discuss four different views of normality. These might be arranged as grades of normality and he concludes that the term normal must be qualified if confusion is to be avoided.

In looking at the chart showing the temperatures of the 276 presumably normal medical students, physiologists and clinicians would be inclined to consider that the 68 per cent within one standard deviation were surely in the normal range. Those readings between one and two standard deviations from the mean might be regarded as probably within the normal range but slightly suspicious. Even for a short distance beyond two standard deviations one could not be categorical in saying that the three students with oral temperatures of 99.1°F. (37.3°C.) had abnormal temperatures. It would be better to take the point of view that the 99.1° reading had one chance in one hundred of being within the normal range.

Table 1 shows the results of several studies on human temperatures but probably does not give the extreme ranges of normal. In general we may accept for rectal and oral temperatures Wunderlich's (2) upper limit of normal as 37.5°C. (99.5°F.) and his sub-febrile range as 37.5°C. (99.5°F.) to 38.0°C. (100.4°F.). The lower limits are not so important since they depend largely on time of day and temperature of the environment. If one were to eliminate the little arrow on the clinical thermoneter and substitute a band marked "Normal Range" Wunderlich's limits of 36.5° - 37.5°C. (97.2° - 99.5°F.) would be conservative and the limits of 36.2° - 37.8°C. (97.0° - 100.0°F.) liberal but not excessive. Either range band would save the mothers much anxiety and relieve the doctor of many calls.

Table 1 is an attempt to find from the literature the average body temperature and the range as measured in normal persons. Some of the readings are rectal, some oral, and a few of the older ones were taken in the well closed axilla. For purposes of calculation we may accept the rectal temperature as standard and consider that the oral and axillary temperatures average about 0.65°C (1.2°F.) lower but there are wide fluctuations. Rarely the mouth and surface readings are a little higher than the rectal. Frequently the mouth readings are two or three degrees lower. From the table it looks as if the classical figure of 37.0°C. for the average rectal temperature is 0.1 to 0.3°C. too high but the matter is relatively unimportant since the average

TABLE 10

Temperature Readings in Normal Subjects

	Average °C.	Lower and Upper Temp. Limits °C.
1. Wunderlich (2) 1868		
Av. for well closed axilla (same as oral)	37.0	
"Really normal temperatures" Axilla		36.6 - 37.4
"Sub-febrile temperatures" "		37.5 - 38.0
"Always very suspicious" beyond "		36.5 - 37.5
2. Pembrey and Nicol (3) 1898		
343 observations on Nicol Rectal	36.79	36.0 - 38.1
377 " " Pembrey Urine	37.01	36.06- 37.83
Rectal temp. above urine Av. 0.26°C. (range - 0.11 to 0.72)		
above oral Av. 0.65°C. (range - 0.33 to 2.56)		
above axilla Av. 0.23°C. (range - 0.06 to 0.33)		
3. Benedict and Carpenter (4) 1910 (Calorimeter)		
8 men with food, 24 hrs. rectal	36.82	35.7 - 37.9
8 men without food, 24 hrs. rectal	36.67	35.5 - 37.7
4 men, 72 days, 528 observations 7 A.M. - 11 P.M. Oral	36.67	
46 men, 84 days, 252 observations 7 A.M. - 6 P.M. Oral	36.83	
"Well within range of physiological limits, lying quietly, rectal		35.9 - 38.1
4. Du Bois (5)		
Men and women in calorimeter 11 A.M. - 2 P.M. Rectal	36.90	36.2 - 37.6
5. Reimann (6) (7) Normal adults Oral	36.8-37.2	36.1 - 37.9
6. Ivy (1) 276 medical students 8-9 A.M. Oral	36.7	35.84 - 37.39
7. Van der Bogert and Moravic (8)		
School children, Oral, 31.4% above 37.3	36.7-37.4	36.1 - 37.8
Children after emotion		38.22
8. Kleitman (9)		
Teen age girl after movies		37.9
Young lady " "		37.6

difference between the low readings in the early morning and high readings in the afternoon is about 1°C.

In addition to individual variations and time of day there are many other factors. Fig. 3 shows that the temperatures of quiet children vary with age and at one and two years average 37.5°C. (99.4°F.). Moderate activity and emotion can easily raise temperatures in children. Hard exercise in athletes can give rectal readings of 39°-40°C. while the mouth temperature is only 36° or 38°C. Exposure to a cold room in the early morning can drop temperatures as low as 36.0° or even 35.5°C. (96.8°F. - 96.0°F.)

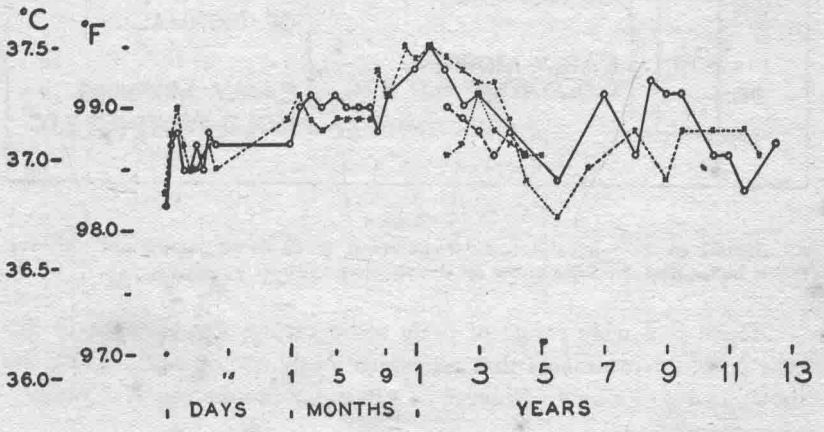

FIGURE 3

Average temperatures of boys (continued line) and girls (dashed line) taken from the monograph of Benedict and Talbot (Carnegie Inst. of Washington, Publ. No. 302, 1921). These were rectal temperatures of children having basal metabolism tests in Boston. Similar rectal temperature readings were made by Lewis, Kinsman and Iliff in Denver on children between the ages of two and five. (Am. J. Dis. Child., 53: 348, 1937.) Boys heavy dashed line. Girls dotted line.

The very low dot at 97.1 F. at the age of 5 is for the only two boys at this age in the Benedict and Talbot series.

Fig. 4 is an attempt to put these figures in graphic form with the realization that the dividing lines are merely approximate. The main point is the fact that normal persons may have temperatures anywhere between 36° and 40°C. (97° - 104°F.) but under ordinary conditions rectal temperatures above 37.5°C. (99.5°F.) should be regarded with suspicion.

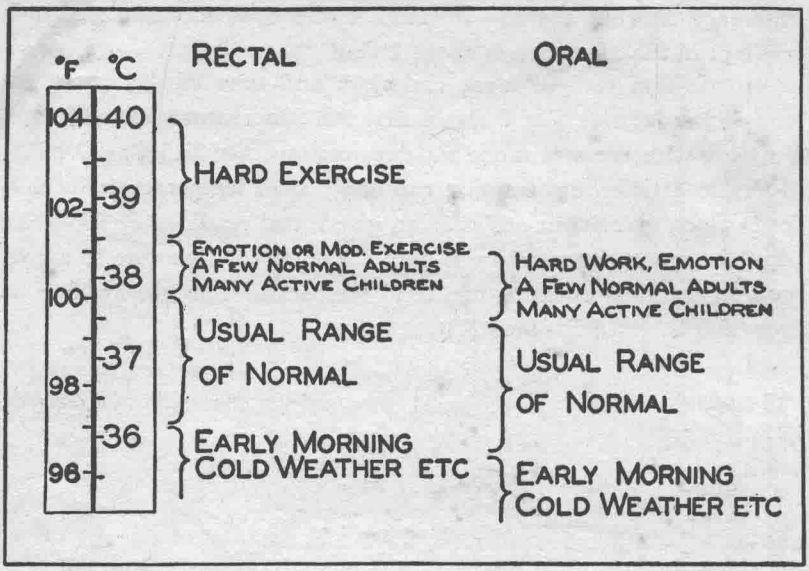

FIGURE 4

An estimate of the ranges in body temperatures found in normal persons. At least this is better than the little arrow on clinical thermometers.

There is a wide range of body temperatures encountered in disease or in environments that are dangerously hot or cold. These are shown in Fig. 5 which will serve as a basis for the discussion of temperature regulation.

Almost everyone thinks in terms of oral temperature. It is easily measured and is good enough for ordinary purposes. Of course the reading will be too low if the patient has cooled his mouth by much talking or has kept the thermometer under his tongue too short a time. Obviously oral temperatures cannot be used with small children or patients who are very sick or delirious. On the medical wards of New York Hospital rectal Centigrade thermometers are employed routinely and readings are made at 7 A.M., 11 A.M., 3 P.M. and 7 P.M. Thermometers are inserted at least two inches and kept in place at least three minutes. More frequent measurements are made if indicated. During late convalescence two oral temperatures a day are considered sufficient.

It is interesting to go through a hospital and find in the various services quite different methods of recordings. In many wards oral temperatures are routine. In some the nurses start taking tempera-

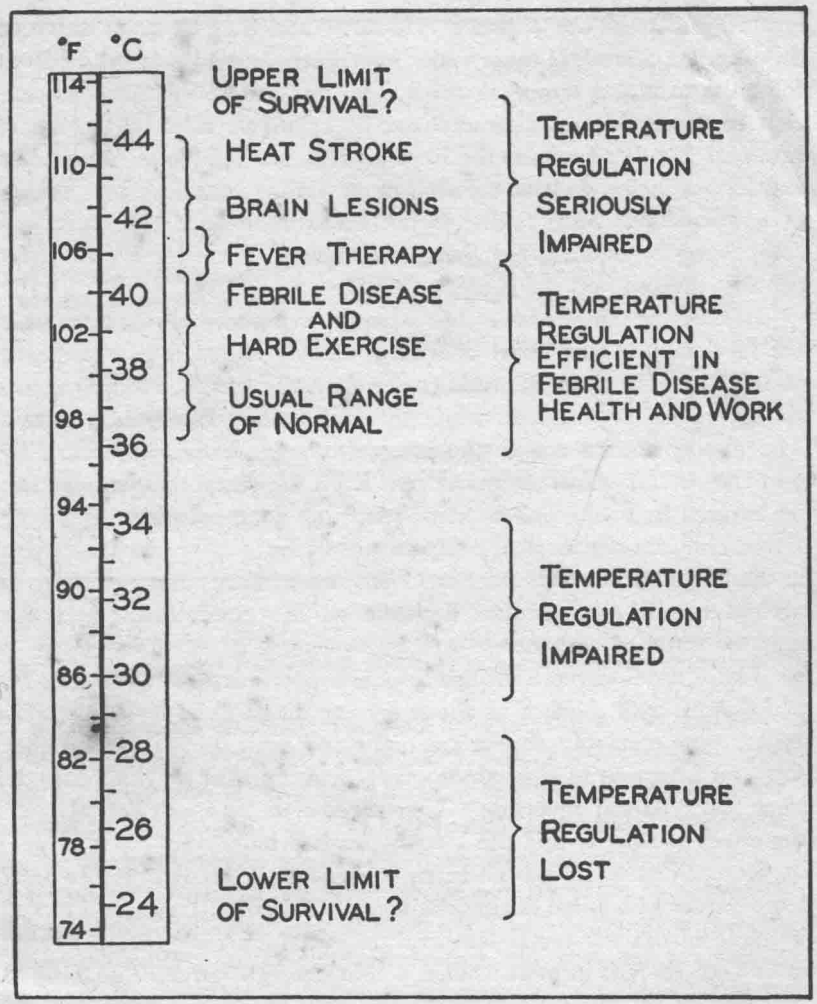

FIGURE 5

Extremes of human body temperature with an attempt to define the zones of temperature regulation.

tures an hour or more before the time at which they are recorded on the chart. Of course no hospital chart with its zigzag lines gives an indication of the fact that the body temperature changes in gradual curves and that the tops and bottoms of these may occur between the hours of recordings.

Another point not generally recognized is that the scales for temp-

erature and pulse are adjusted arbitrarily and may be quite different on different charts. If these scales have been well adjusted the curves for pulse rate and temperature changes are almost superimposed except in those diseases characterized by relatively slow or fast heart rates. If in other patients the lines diverge markedly one suspects an extraneous factor such as emotion or an error of reading or a faking of temperature. Such faking is not uncommon and it is easily accomplished by holding the thermometer near some hot object or by rubbing the bulb on the sheet.

It must be emphasized that a single temperature reading gives the level in one small part of a large body. The skin and the mass of subcutaneous tissue is much cooler than the rectal area and it can change in either direction while the rectal temperature is constant. The mouth reflects chiefly the internal average but is influenced by skin and subcutaneous temperatures. Even the rectal temperature can be lowered by cool blood in veins returning from cold legs.

In children the normal temperature is much more variable than in adults and tends to be higher. With small infants and especially in prematures the temperature depends on the environment and this must be watched with care.

The diurnal curve with the lowest temperatures between 2 A.M. and 6 A.M. is established at about the age that a child learns to walk. When some men start to work at night and sleep during the day they show an inversion of this curve, others maintain the original pattern, some have partial inversion. There seems to be a conflict between the effect of activity and the long established habit.

Recently there have been many reports on the changes in the basal temperature of women during the menstrual cycle. If a careful record is made of oral or rectal temperature every morning before getting out of bed there is in most women a characteristic curve. The temperature drops about 0.6°C. (1.°F) a few days before the onset of menstruation rises slowly, maintains a level until about the 14th day when there is a brief fall of about 0.2°C, usually unobserved, and then a rise to a level about 0.3° C. above its previous height. This drop and subsequent rise takes place at the time of ovulation. Not all women show this phenomenon.

Thermal Balance

The basic factors concerned in the balance of heat production and heat loss can best be demonstrated in a diagram (Fig. 6). Heat pro-

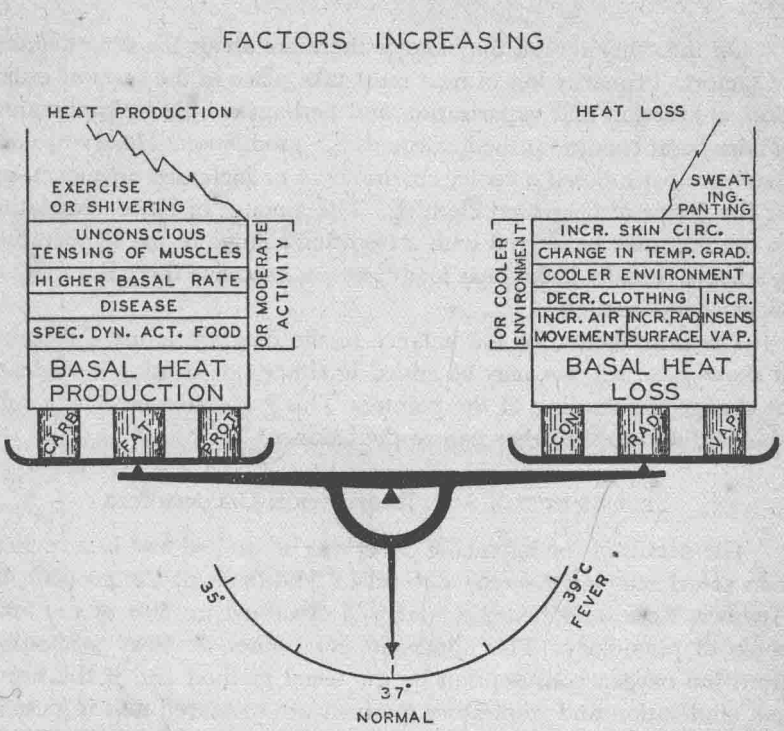

FIGURE 6

Balance between factors increasing heat production and heat loss. (Du Bois, Harvey Lecture, Bull. N.Y. Acad. Med., 1939.)

duction is furnished to the body by protein, fat and carbohydrate. For our purposes we do not need to consider the complicated details of their metabolism since they furnish to the body the same amount of heat that is liberated when they are oxidized in a bomb calorimeter if due allowance is made for waste products. Carbohydrate and fat are the chief sources of energy and there is always a small reserve of carbohydrate in the form of glycogen and a large reserve of body fat. During the major portion of the night when the person is sleeping the production is at the basal level but during the day, except for periods of complete rest, there are the factors of moderate activity and the specific dynamic action of food. Food causes an average rise of about six per cent above the basal level. Severe exercise can increase the metabolism ten or twelve times the basal level. In conditions of moderate cold there may be an unconscious tensing of muscles and in extreme cold a bout of involuntary shivering that raises heat production two or three times the basal level.