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THE
CROONIAN LECTURES

W. HALE WHITE

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THE
MEANS BY WHICH THE TEMPERATURE
OF THE BODY IS MAINTAINED IN
HEALTH AND DISEASE

BEING

The Croonian Lectures

DELIVERED BEFORE

THE ROYAL COLLEGE OF PHYSICIANS OF LONDON

On June 15th, 17th, 24th, and 29th, 1897

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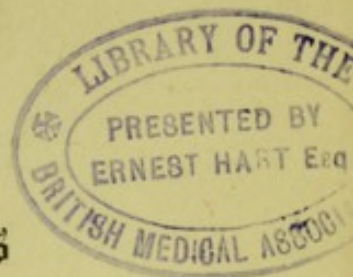
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The Croonian Lectures
ON
THE MEANS BY WHICH THE TEMPERATURE
OF THE BODY IS MAINTAINED IN
HEALTH AND DISEASE.

LECTURE I.¹

MR. PRESIDENT AND GENTLEMEN,—In the first place I have to express my very best thanks for the great honour which our late President, Sir Russell Reynolds, conferred upon me when he invited me to deliver the Croonian Lectures before this College. After I had said I would deliver them I looked down the list of my predecessors, and since I saw how distinguished a list it is I have often regretted my boldness, and I can assure my hearers that no one is more fully aware than I am of the many deficiencies in the lectures I am about to give.

I propose in them to discuss the details of the means by which the temperature of the body is maintained in health and disease. My hearers will find that many points are omitted, but when they call to mind the great complexity of the subject and the scantiness of our knowledge they will, I am sure, forgive me.

I have purposely avoided the word "fever" in the title of these lectures, for it lacks exactitude. It is an admirable word, but it has been handed down from a time when less was known than we know now and when the clinical thermometer was not employed. As we use it to-day it is difficult to define in such a way as to cover every use of it, but probably most of us mean by it to designate a certain assemblage of symptoms which follow the introduction into the body of certain poisons; thus, when an unprotected person is inoculated with small-pox he shows certain symptoms, and is therefore said to have a fever. One of the most prominent of these is pyrexia, but pyrexia may occur, as I shall show, if we remain a long while in a hot bath, or as a result of cerebral hæmorrhage. Probably there are some of us who would not consider the man who had had a very hot bath or the man who had a cerebral hæmorrhage to be suffering from fever, but a study of the raised temperature in these conditions will help us to understand the pyrexia

¹ Delivered on June 15th.

which occurs in cases to which everyone is agreed the term "fever" may be applied. Another reason for confining ourselves in these lectures to pyrexia rather than fever is that this term includes so many symptoms—e.g., rapid pulse and rapid respiration—that we should not have time to consider them all.

Before studying pyrexia experimentally there are some pitfalls of which we must beware. In the first place, the normal range of temperature in the lower animals is wider than in man. I have very often taken the rectal temperature of rabbits, dogs, and monkeys, and have found the range to be greater than in man. I have compiled from Dr. Pembrey's article on Animal Heat in Professor Schäfer's forthcoming "Physiology" the appended table (Table I.), which shows very well the range of temperature in different animals.

TABLE I.

Animal.	Average rectal temperature.	Extremes of observations.	Number of observations.
	Degrees C.	Degrees C.	
Horse	37·8	36·1—38·6	962
Cow	38·7	37·5—39·4	116
Sheep	40·4	38·5—41·8	304
Dog	39·0	37·1—39·9	250
Cat	38·7	37·9—39·7	41
Pig	39·2	38·7—40·8	269
Rabbit... ..	38·9	37·0—40·8	110
Guinea-pig	37·9	37·0—39·2	19
Rat	37·5	37·0—38·5	16
Mouse	37·4	37·1—38·6	27
Monkey (Rhesus) ...	38·4	36·9—39·7	22

In the next place the prolonged administration of an anæsthetic causes a fall of temperature. Thus, Pembrey² has proved that the temperature falls in anæsthetised mice, and Binz,³ quoting from Kappeler, says that after the administration of ether to human beings the bodily temperature sinks from 0·3° to 1·5° C. (the mean of twenty etherisations was 0·68° C.); but it rises again in a few hours to normal. Twenty-three observations were made on the effect of chloroform on human beings, and it was found that on the average the temperature fell 0·53° C. The fall did not begin till at least twenty minutes after commencing inhalation and was

² Proceedings of the Physiological Society, Feb. 16th, 1895.

³ Lectures on Pharmacology, Sydenham Society translation, vol. i., p. 11.

generally most marked after narcosis had passed off. In from twenty minutes to five hours the normal temperature was regained. Binz, quoting from Scheinesson, says that anæsthetics do not increase the dissipation of heat, and he considers that they directly diminish the power of the body to produce heat. But in rabbits at least I can, from personal observation, state that if the anæsthetic is only given for two or three minutes no appreciable alteration of temperature takes place.

Another fallacy to be avoided in the experimental study of pyrexia is that the performance of artificial respiration will by itself cause a considerable alteration of temperature. This is particularly unfortunate, for at first sight it seems as though we might learn much about pyrexia from a study of the behaviour of the temperature when the spinal cord is cut or curare has been given; but as in either case artificial respiration would be necessary these modes of experiment are closed to us. Le Gallois⁴ as long ago as 1817 showed that artificial respiration depressed the temperature, and also that to a less extent anything—such as tying an animal down—which hindered respiration caused the temperature to fall. Dr. Fawcett and I in the course of some experiments we were conducting on the physiological action of β -tetrahydro-naphthylamine made some observations upon the combined effect on the temperature of etherisation and artificial respiration. Rabbits were used, the animal was kept fully under ether for two hours, and during this time it was fixed to a board in the usual way, and artificial respiration was carried on through an opening in the trachea. The following table (Table II.) shows the results we obtained.

TABLE II.

Number of experiment.	Fall of temperature.	Hours during which it fell.	Remarks.
	Degrees C.		
1	4.8	3½ hours.	These two animals were wrapped in cotton-wool.
2	2.2	2¼ "	
3	3.4	3¼ "	

It will be seen that the depression of temperature was very considerable and that it could not be prevented by wrapping the animal in cotton-wool. It is clear, therefore, that as the combined influence of ether, artificial respiration, and fixing a rabbit to a board produces such a marked fall in the animal's temperature, this method of experiment is quite inapplicable for working out problems dealing with the varia-

⁴ Annales de Chimie et de Phys., IV., 1817.

tions of temperature of rabbits. We may now leave the fallacies and pass on to the chief subject of these lectures.

The fundamental problem in a study of pyrexia is to discover whether or not the production of heat is increased, for it is clear that the temperature of the body may rise either because the loss of heat from it is less, while the production remains the same, or because the loss of heat remains the same while the production of heat is increased, or, if both vary, because the variations in the production have not been exactly counterbalanced by variations in the loss. The opinion of the profession upon the question whether in fever the rise of temperature is due to a diminution of the loss of heat, or an increase of production has varied in accordance with the views of our most distinguished pathologists. Thus Traube taught that the rise of temperature in fever is due to a contraction of the superficial arterioles, there being then less blood in the skin, the body consequently loses less heat by radiation and conduction and hence its temperature rises. Liebermeister, on the other hand, taught that the increased temperature in fever was due to a greater production of heat. But it appears to me to be possible that the discussion has in a sense been beside the mark, for we know that most, if not all, fevers are due to the circulation of poisons in the blood, and there is no reason why we should believe that they all produce pyrexia in the same way. All collateral evidence is against such a view; many poisons accelerate the beat of the heart, but some act upon the vagus, others upon the accelerator nerves; many poisons produce diaphoresis, but jaborandi acts upon the peripheral terminations of the sudoriparous nerves while opium acts centrally. And I hope I shall, in these lectures, be able to bring forward evidence to show that sometimes pyrexia is due to an increased production of heat and sometimes to a diminution of the loss. If this can be done it will put an end to the discussion as to whether in fever the production of heat is increased or the loss diminished; but we shall have to discuss the question for each separate febrile disease.

Before, however, doing this I should like to call attention to a point that I have never seen discussed—namely, whether there is any evidence that pyrexia may be due to a variation in the specific heat of the body. It takes more heat units to warm to a given temperature a body with a high specific heat than it does to warm a body with a low specific heat to the same temperature, so that if the specific heat of the human body diminished while its production and loss of heat remained the same its temperature would rise; and at first sight it appears that this would be a most economical way of raising the temperature, as there would be no extra expenditure of energy in increasing the production of heat; but perhaps the alteration of the specific heat of the body might entail such considerable molecular change that it would necessitate an expenditure of energy. Most observers have estimated the specific heat of the body by calculation after death from that of the various tissues of the body. The

lowest estimate given by this method is 0.75, the highest 0.9; but this is what might have been expected when we remember that a large proportion of the body is water. The properties of dead and living bodies are so unlike, and the specific heat of complex substances is often so difficult to foretell, that I thought it would be worth while to see if some means could be devised of estimating the specific heat of living animals. This would be easy enough in the case of cold-blooded animals by observing the relative number of degrees of temperature through which the animal and an equal weight of distilled water originally at the same temperature rose or

TABLE III.—*Weight of Dormouse 13.55 grammes.*

Time.	Temperature of dormouse.	Temperature of equal weight of distilled water.	Specific heat from these figures.	Temperature of room.
	Deg. F.	Deg. F.		Deg. F.
9.10 A.M.	37.5	37.5		37
	Both brought into a warm room.			
9.35 "	43	42	$\frac{4.5}{5.5} = 0.818$	50
10 "	47	46.25	$\frac{3.75}{9.5} = 0.921$	50.5
10.30 "	48	47.25	$\frac{9.75}{10.5} = 0.928$	51.5
11 "	49.25	48.25	$\frac{10.75}{11.75} = 0.915$	52
	Both taken into a cold room.			
11.30 "	43	43	$\frac{5.25}{6.25} = 0.840$	37
11.50 "	40.75	40	$\frac{8.25}{8.5} = 0.970$	37
12.30 P.M.	39	38	$\frac{10.25}{10.25} = 1.0$	37

fell when both were, under exactly similar conditions, subjected to warming or cooling, for it is well known that the temperature of cold-blooded animals rises and falls with that of their surrounding medium. But the thermic mechanism of warm- and cold-blooded animals is so different that it would be rash to assume that the specific heat of warm-blooded animals is the same as that of cold-blooded animals.

It struck me, however, that by using hibernating mammals it would be possible to calculate the specific heat of living animals not far removed from man. I employed dormice, for they are easy to obtain and to observe. When hyber-

nating they lie tightly curled up in a ball, with their feet tucked away in the centre of the ball, and it is easy to take their temperature by placing the bulb of a thermometer in the centre of the ball. The first point to determine was whether when they are hibernating their temperature rises and falls with that of the surrounding medium. The figures given in Tables III. and IV. show that it does. For example, it will be seen in Table III. that when the temperature of the room was 37° F. that of the dormouse was 37·5°, and that when it was brought into a

TABLE IV.—*Weight of Dormouse 13·5 grammes.*

Time.	Temperature of dormouse.	Temperature of equal weight of distilled water.	Specific heat from these figures.	Temperature of room.
	Deg. F.	Deg. F.		Deg. F.
10.59 A.M.	40	40	—	40
	Both brought into a warm room.			
11.15 "	43·5	43	$\left\{ \frac{3.0}{3.5} = 0.857 \right.$	50
11.40 "	46	45·5	$\left\{ \frac{5.5}{6.0} = 0.917 \right.$	51
11.55 "	47·5	47	$\left\{ \frac{7.0}{7.5} = 0.933 \right.$	52
12.7 P.M.	48	48	$\left\{ \frac{8.0}{8.0} = 1.0 \right.$	52
12.30 "	49.5	49.5	$\left\{ \frac{9.5}{9.5} = 1.0 \right.$	52
	Both taken into a cold room.			
12.57 "	44	43	$\left\{ \frac{6.5}{5.5} = 1.182 \right.$	36
1.10 "	43	42	$\left\{ \frac{7.5}{6.5} = 1.154 \right.$	36

room at 52° its temperature slowly rose till it was 49·25°; it was then put back into the cold room and its temperature slowly fell. A large number of observations gave similar results; but the experiment requires to be made with considerable care for many reasons, each of which will be found in a paper which I published.⁵

The method of experimenting was as follows. The hibernating dormouse was carefully weighed. It was then placed on the bottom of a thermometer stand, exactly like an ordinary test-tube stand in which the test-tube

⁵ Journal of Physiology, Supplementary Number, 1892.

stands mouth upwards, except that the holes were only large enough to take a thermometer. The bulb of a thermometer was left buried in the centre of the ball formed by the hibernating dormouse. A number of cubic centimetres of distilled water equal to the weight of the dormouse in grammes were then measured into a very thin, bright, platinum vessel, which had been made to hold just about the right amount. This vessel with its contained water was placed on the bottom of the test-tube stand as far removed from the dormouse as possible. A thermometer was placed in it. The temperature of the surrounding air close to the thermometer stand was observed. All three thermometers had been tested beforehand to see that they gave similar readings. Sufficient time was allowed for all three thermometers to become steady. The thermometer stand with the dormouse and the water on it were then taken into a room of a temperature about 50° F., and the readings given by the thermometer which was buried in the dormouse and by that in the water were noted from time to time. When that of the dormouse was about 50° F. the thermometer stand was moved back into the cold room and the readings were again noted. It is clear that as the temperature of the dormouse rose and fell with that of the air, the number of degrees an equal weight of distilled water rose or fell divided by the number of degrees the temperature of the dormouse rose or fell in the same time will give the specific heat of the dormouse. I performed many experiments and found that, calculated in this way, the specific heat of the dormouse varies between 0.812 and 1.18, so that if we set it down at 0.95 we shall probably be very near the mark. It is noteworthy that when the thermometer stand was first brought into a warm room the earlier observations always gave a slightly lower specific heat for the dormouse than the later ones, because at first the rise of the temperature of the animal was, in comparison with the rise of that of the water, slightly the faster. The consequent slight increase in the creature's specific heat was often uniform. Thus in Table IV. the first observation gave a specific heat of 0.857; according to the second it was 0.917; according to the third it was 0.933; and according to the fourth it was 1.0. Another noteworthy fact is that if the specific heat was calculated from observations made when the thermometer stand had been removed from a warm room into a cold one, it was always slightly higher than if calculated from observations made when the stand was brought from a cold into a warm room, and also the earlier observations gave the lower specific heat.

The close agreement of these results with those obtained by calculation from the dead tissues shows, I think, that we may safely put down the specific heat of dormice as being slightly below that of water. There are in these experiments several possible fallacies, but I think I have shown, in the paper referred to, that they are unimportant. Because of these unavoidable fallacies the specific heat obtained by this method is only approximately accurate, but reference to the

paper just mentioned will show that the fallacies lead to only a slight error, and that on the whole the specific heat calculated by this method is slightly too low. Probably the results are more accurate than those obtained by calculating the specific heat of each of the tissues of the dead body and from these results estimating the specific heat of the body as a whole. It will be observed that the figures obtained by the two methods are in close accord, but that by the method here given the specific heat appears higher than when calculated from the dead tissues.

I should not have introduced these figures had I not wished to show that whether we calculate from dead or living tissues the specific heat of the body is high, and it is obviously an advantage for warm-blooded animals, having, as they have, to maintain a constant temperature, to have a high specific heat, for bodies with a low specific heat cool much more readily when the temperature of the surrounding medium falls than do those with a high specific heat; and although it would be unfair to definitely apply results obtained from hibernating dormice to a man suffering from fever, I think we may say that at present there is no evidence that in man the rise of temperature is due to a diminution of the specific heat of the body, as whatever the temperature of these dormice their specific heat varied very little, for reference to the paper from which I have quoted will show that experiments conducted for the same time usually gave nearly the same specific heat. Further, there is no reason to believe that the human body disobeys the law that the specific heat increases with the temperature and therefore until the contrary is proved we must suppose that, other things being equal, it takes a few more calories of heat, and therefore requires a greater production of heat to raise the temperature of the body from 104° to 105° than it did to raise it from 98° to 99° .

We now pass on to a consideration of the question whether or not in pyrexia the production of heat is increased or the loss diminished. There are three ways by which this may be investigated:—(1) By comparison of the variations in the loss of heat with the variations of internal temperature; (2) by calorimetry; and (3) by chemical means; and it will be convenient if we consider them in this order.

1. COMPARISON OF THE VARIATIONS OF THE LOSS OF HEAT WITH VARIATIONS OF INTERNAL TEMPERATURE.

The communication which Dr. Waller made to the Physiological Society on Nov. 11th, 1893, suggests the possibility of easily finding out whether in man the production of heat is increased when the temperature is raised, and of studying in detail the means employed to keep the

temperature constant in health. It is clear that when the surface temperature of the body rises the loss of heat by radiation and conduction will be increased, and that when the amount of sweat secreted is increased the loss of heat from evaporation is increased, so that if in any case it can be shown that the internal temperature has risen, and at the same time the surface temperature has risen and the amount of sweat secreted has increased, the production of heat must have increased, provided that the temperature of the surrounding air is constant, and in the wards of a hospital it is kept nearly so. I will now describe the means I have employed to obtain these data.

The internal temperature.—This is taken with an accurate self-registering clinical thermometer. When only slight variations are expected it should be taken in the rectum or the axilla, for the rapidity of respiration and the temperature of the respired air affect the mouth; but when, as in many cases of fever, the temperature is raised several degrees above normal, an observation taken in the mouth will suffice, and if the observer is single-handed it is a great convenience to take it in the mouth, for the internal temperature, that of the surface, and the amount of sweat secreted should all be observed simultaneously.

The surface temperature.—This should be taken with a flat-bulbed thermometer held gently on the skin until the index is stationary; if it be held too firmly the pressure exercised will send up the mercury. Suitable thermometers can be obtained from A. Deane, of Hatton-garden. The skin of the abdomen near the umbilicus is the best place to take the temperature, for whether the person observed have his clothes on, or whether he be in bed, the skin here is less liable than that elsewhere to transient variations of temperature from exposure to currents of air. The temperature registered by the thermometer does not represent that of the skin with absolute accuracy, for part of the bulb is exposed to the air, and the skin covered by the bulb slowly gets warmed because the bulb protects it, but as my object has always been to obtain comparative, not absolute, results these errors are of no importance. The following observation demonstrates very well that these thermometers readily show variations of surface temperature. I exposed the extensor surface of my forearm for some hours to the sun, the vessels consequently dilated, and the part was red, the surface thermometer showed the temperature at a spot well inside the margin of the red area to be 34.25°C ., one-third of an inch outside the margin—the vascular dilatation here being just visible—it was 33.25° ; and some distance from the red patch the temperature was 32.5° . I have tried this experiment several times and the differences are always well shown. It is of interest to observe that even extreme vascular dilatation quite as great as is observed in any fever, only increased the surface temperature of the skin 1.75°C .

☞ *The estimation of the sweat.*—This was estimated by using calcium chloride as an absorbent. It was fused into the bottom of a shallow circular glass box. All the boxes used in the observations had air-tight lids, and the inside diameter of all was the same—viz., 4.5 c.m.—and therefore the area of the bottom of each box was 15.9 square c.m. The inside depth was about 2 c.m. The best way to make the calcium chloride adhere to the glass is to take fine pieces of it, place them in the bottom of the box, and then add a trace of absolute alcohol. The box is then put into an oven, which is slowly heated so that in an hour it is 150° C., and then the oven is left to slowly cool again. The absolute alcohol contains minute traces of water, and this is just sufficient to soften the edges of the pieces of calcium chloride enough to agglutinate them, and this water is driven off by the heat; the alcohol, too, acts as a slight solvent. When a reading is taken the box is held inverted on the skin for a given time (in the observations I have made I have, except in a few preliminary cases, always held it for ten minutes) and the difference in its weight before and after gives the amount of sweat secreted. It is best held with one finger so that the heat of the hand shall not affect it. To obtain accurate results the boxes must not be weighed directly after they are removed from the skin, for the glass has been warmed by the skin, consequently it displaces more air and warm air currents proceed from it while it is on the pan of the balance, and I always found that as it cools its weight slowly increases.

The following figures, Table V., show this. I tightly held

TABLE V.

Weight of box and lid before box was put in } the palm } Weight of box and lid directly after box was } taken off at 9.45 P.M. }	75.4593 grms. 75.4625 ..
Gain	0.0032 grms.
Weight at 10.15 P.M.	75.4644 grms.
Weight at 10.45 P.M.	75.4652 ..
Weight at 11.30 P.M.	75.4658 ..
Weight at 11.45 P.M.	75.4658 ..
Total Gain	0.0065 grms.

the box with its lid off inverted on the palm of one hand, pressing it down with the palm of the other for five minutes, so that it was completely shut up in the clasped hands. Directly the five minutes was up the air-tight lid was put on the box. This table shows that the amount of sweat secreted from the palm in five minutes really was 6.5 milligrammes, not 3.2 milligrammes, as a reading taken at once would

appear to show, and the weight of the box and lid did not become constant until more than an hour had elapsed from the removal of the box from the hand. But this was an extreme experiment, the box was warmed considerably by being grasped in the closed hands. When it is held on with one finger the weight becomes constant in half an hour, and probably often in less. The following figures show this (see Table VI.).

TABLE VI.

Weight of box and lid before box was put on } the palm }	81.6438 grms.
Weight of box and lid directly after it was } taken off, 10 P.M. } <hr/>	81.6432 ,,
Gain	0.0044 grms.
Weight at 10.30 P.M.	81.6499 ,,
Weight at 11 P.M.	81.6499 ,,
<hr/>	<hr/>
Total gain	0.0061 grms.

Here an immediate weighing appeared to show a gain of only 4.4 milligrammes, but the gain really was 6.1 milligrammes. Therefore it is clear that to get accurate results the boxes must not be weighed till some little time after they are removed from the body. When the box is weighed before the observation it contains air at the temperature of the room, but when it is inverted over the skin it contains warm rarified lighter air, and as the box itself is warm after it is taken off the skin the air in it when the lid is put on is still rarified, and when it is weighed, as the cover is air-tight, it still contains lighter air than it did before the experiment began. To show this I just lifted the lid and instantly closed it again, when after an experiment the box had been left till its weight was constant. For example, in the last experiment detailed the box weighed 81.6499 grammes. The lid was lifted and immediately closed again; the box then weighed 81.6501 grammes, a gain of 0.2 milligramme. As other experiments also showed that the gain was only 0.1 or 0.2 milligramme it is clear that no account need be taken of this varying density of the air, especially as some of this gain that is only shown in the fourth place of decimals may be due to absorption of moisture from the air let in.

Another possible source of error is the condensation of moisture on the boxes; but the amount in the air in a room does not vary much in three quarters of an hour, and the box was not weighed after an observation until its temperature had become the same as it was when it was weighed before the experiment, so that this source of error is not important. It can, however, always be avoided by having in one pan of the balance a dummy empty box exactly like the one used for experiment, and weighing one

against the other both before and after the observation and noting the excess of the difference between the weights of each box. It would probably not be desirable to invert the empty dummy box on the skin at the same time as the box containing calcium chloride and leave both boxes on for the same length of time close to one another, and then to weigh them one against the other immediately after; for though they would both have been warmed by the skin, yet we have seen that the error due to this warming of the boxes may be so considerable that if the two boxes had not taken up equal amounts of heat from the skin the result of observing the alteration of the difference in their weights would not be trustworthy, and it is unlikely that they would have taken up equal amounts, for one box has calcium chloride in it and the other has not, and the amount of glass in the boxes is variable. But whether the method of dummy boxes be adopted or that, which is probably more accurate, of leaving an air-tight box to cool, an air-tight lid is a necessity; for if it is not used the results will be inaccurate, because the calcium chloride will absorb moisture during each weighing, and also if no lid is used the observation must be carried on directly opposite the balance, and immediately after the box is weighed it must be put on the skin, and immediately after it is taken off it must be again weighed; but in clinical work the balance can hardly be carried to the bedside of each patient. The lids of the boxes I used fitted on like a cap, and where the lid came in contact with the box the glass of each was finely ground; if then the merest trace of vaseline was put on the ground glass the boxes became quite air-tight enough. This I proved over and over again by leaving the boxes with calcium chloride in them but with the lids on about the laboratory, and weighing them at intervals of some hours. For instance, six such boxes were left in the laboratory for twenty-six hours during which the air happened to be nearly saturated. The gains in weight are shown in Table VII.

TABLE VII.

Box 1 gained	0.0001	grm.	in twenty-six hours.		
" 2 "	0.0002	"	"	"	"
" 3 "	0.0003	"	"	"	"
" 4 "	0.0006	"	"	"	"
" 5 "	0.0008	"	"	"	"
" 6 "	0.0010	"	"	"	"

On another occasion two boxes gained in weight in twenty-six hours 0.1 and 0.2 milligrammes respectively. It is clear, therefore, that if the boxes are weighed within an hour or two of an observation there is no appreciable error due to absorption of moisture from the air. In the next lecture we will consider some examples of this method.

LECTURE II.¹

MR. PRESIDENT AND GENTLEMEN,—You will remember that in the last lecture we saw that it would be possible by taking simultaneous observations of the internal temperature, the surface temperature and the amount of sweat secreted, to find out in man whether a rise of internal temperature was due to a diminution in the loss of heat or an increase of the production. Further, it is clear that this method will enable us to tell the cause of the fall of a high temperature. The experiments that I am about to detail to you were carried out with these objects. The temperatures are all given in degrees Fahrenheit, and the amount of sweat in milligrammes.

A. Temperature raised by a hot bath; experiments on myself (see Table VIII.).

The temperature rises in these experiments owing to the fact that the hot water stops the loss of bodily heat by radiation and conduction, and it prevents evaporation of sweat. Probably the hot water does not warm the body much in so short a time as the specific heat of the body is high. In both these experiments I could, by watching the skin, see that the secretion of sweat did not begin to be very profuse till a few minutes after I was out of the bath, but by ten minutes after it was extraordinarily abundant. It will be seen that in all respects the first bath produced more marked effects than the second; probably this was because the second cooled the faster. But both experiments teach that the evaporation of sweat is by far the most important agent in reducing the bodily temperature when it has been artificially raised by a bath, and it will be noticed that when such a large amount of sweat is secreted the surface temperature is lower than it was either before the experiment began, immediately after the bath, or some time after the experiment, when the secretion of sweat is nearly normal. This is no doubt due to the rapid evaporation of the sweat, and this means of reducing the temperature is so energetic that it actually makes the loss by radiation and conduction less, although the internal temperature is raised; it will be seen that in the first experiment the surface temperature fell 5.8° in ten minutes, but in the second with much less sweat secreted it only fell 1.9° in fifteen minutes. Other striking facts are the rapidity with which a normal temperature is regained and the enormous quantity of sweat secreted.

¹Delivered on June 17th.

B. *Temperature raised by Turkish bath; experiment on myself.*—Before the bath the mouth temperature was 98.8° , and the surface temperature of the abdomen was 90.5° . Milligrammes of sweat from the abdomen in 10 minutes 2.2. After taking these observations I went into the hot rooms and remained there an hour and twenty minutes,

TABLE VIII.—*Temperature Raised by Hot Bath.*

Number of experiment.	Time.	Mouth temperature.	Abdominal surface temperature.	Milligrammes of sweat from abdomen in ten minutes.	Remarks.
	P.M.	Deg. F.	Deg. F.		
1	7.0	98.2	93.7	2.4	Got into hot bath (temperature 112°); remained in fourteen minutes. When I came out I felt faint, breathing deeply. The bath was then 108° . I rapidly dried myself, put on dressing-gown, and lay down.
	7.25	—	—	—	
	7.45	103.2	94.5	185.7	
	7.55	—	88.7	—	
	8.5	99.5	—	—	
	8.15	98.6	—	—	
	9.0	98.0	92.8	2.3	
2	3.30	98.2	92.8	1.5	Got into hot bath (temperature 112°); remained in fourteen minutes. The bath was then 106° . Faintness and rapid breathing were not so marked. Dried as before.
	3.40	—	—	—	
	4.0	101.0	93.7	92.4	
	4.15	—	91.8	—	
	5.0	98.2	93.7	3.9	

mostly at 120° , but for some time in rooms at 150° and 190° . Then I was massaged, shampooed, and had a shower bath. After which I was wiped quite dry, and then the mouth temperature was 99.8° , and the surface temperature of the abdomen was 92.3° . Milligrammes of sweat from the abdomen in ten minutes 46.1. Here, again, we see what a very

energetic agent sweating is in reducing an artificially raised temperature, for after I had been sweating profusely for eighty minutes in the bath the sweat was still being secreted twenty times as fast as before the bath, but the quantity was not enough to make the surface temperature lower than before the bath.

C. *Temperature raised by damage to the brain.*—In two papers² I have shown that damage to the corpus striatum in rabbits raises their internal temperature. So many experimenters have confirmed this observation that I need not now trouble you with the details. The following table (Table IX.) shows the results I obtained in twenty-seven experiments.

TABLE IX.

Highest temperature after operation.	No. of degrees above that immediately before.	Highest temperature after operation.	No. of degrees above that immediately before.	Highest temperature after operation.	No. of degrees above that immediately before.
Deg. F.	Deg. F.	Deg. F.	Deg. F.	Deg. F.	Deg. F.
106·8	5·2	105·4	2·0	104·2	1·1
106·8	4·6	105·4	2·4	104·0	1·8
106·7	4·5	105·2	4·0	103·6	2·7
106·2	3·2	104·9	3·1	103·6	0·6
106·0	3·6	104·8	3·6	103·4	2·0
105·0	3·7	104·6	2·4	103·0	- 0·2
106·0	4·7	104·4	2·2	100·8	- 0·4
105·9	3·3	104·4	2·0	—	—
105·8	4·8	104·2	2·0	—	—
105·6	4·4	104·2	1·2	—	—

In the last experiment the lesion was very extensive, and the fall of temperature was due to loss of blood. I show you a chart in which you can see very well the rise of temperature produced in a rabbit by damage to the corpus striatum (see Chart 1).

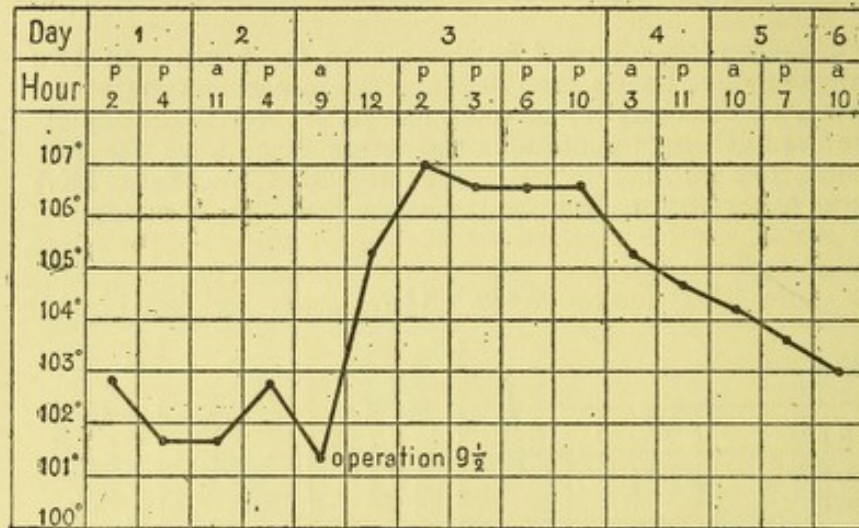
Many instances in which in man after a hæmorrhage into the corpus striatum the temperature has been raised have been recorded by Bourneville, Ferrier, J. H. Bryant, myself, and others, and references to these authors will be found in an address I gave at a meeting of the British Medical Association at Bristol in 1894.³ These cases show that if after a hæmorrhage takes place into one corpus striatum the

² Published in the *Journal of Physiology*, vol. xi. and vol. xii.

³ *Brit. Med. Jour.*, Nov. 17th, 1894.

temperature is raised, it will be higher in the opposite or paralysed axilla than in the axilla on the non-paralysed side, and that the temperature on the paralysed side remains

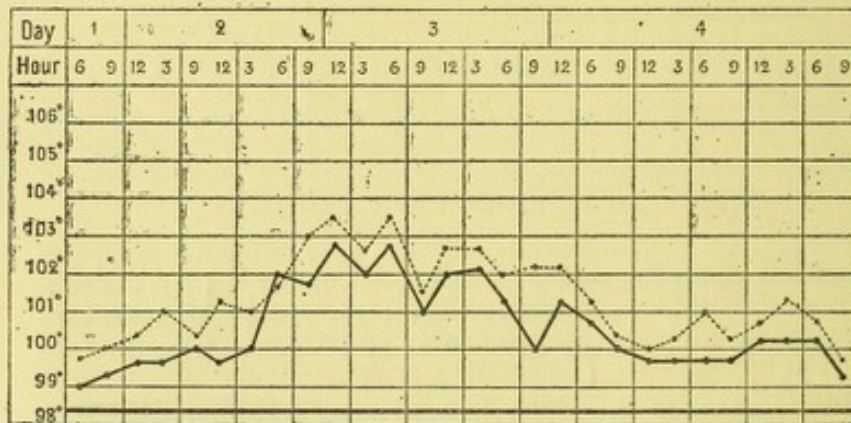
CHART 1.



Shows the rise of temperature in a rabbit after damage to the corpus striatum.

higher than that on the other even during the subnormal period which succeeds the rise. I have seen several cases which illustrate this, and I will show you charts of two of

CHART 2.

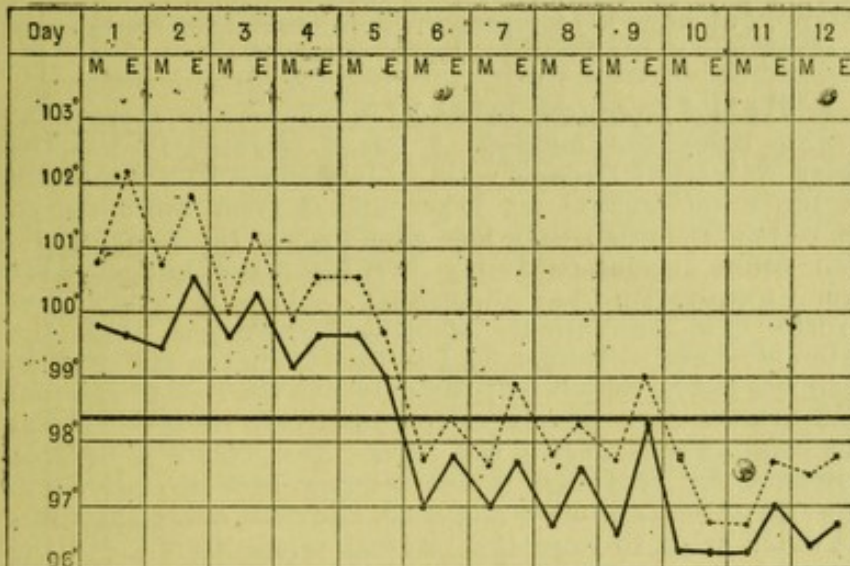


Shows the temperature after hæmorrhage into the corpus striatum on one side. The dotted line shows that in the axilla on the side opposite to the hæmorrhage; the straight line that on the same side as the hæmorrhage. (From a patient in Mary ward.)

them (see Charts 2 and 3), and since I began to investigate surface temperatures two more such cases have come under my care. They gave the following results (see Table X.).

It will be seen that in both these cases the temperature was always higher in the paralysed axilla—that is to say, the internal temperature was higher on the paralysed than on the sound side. In the first case the surface temperature of the two arms was equal, but the amount of sweat secreted on the paralysed arm was much greater than on the other, therefore the loss of heat must have been more rapid on the paralysed side; but as in spite of this the internal temperature was raised, the quantity of heat in the paralysed arm must have been greater than that in the unparalysed arm. In the second case on one occasion the secretion of sweat was almost equal on the two arms and on two other occasions it was greater on the paralysed side. The surface temperature was always considerably greater on the paralysed arm, so that here the losses from evaporation, radiation and

CHART 3.



From another but similar case to the preceding.

conduction are all greater from the arm with the higher internal temperature; therefore in this case, too, the quantity of heat must have been considerably greater in the paralysed arm than in the other. In neither case was there any visible dilatation of the vessels on the paralysed side, nor have I ever observed, even when the difference of temperature has been considerable, any dilatation of the vessels on the paralysed side in hemiplegia. This is evidence against the view that the increased temperature on the paralysed side is due simply to there being more blood in the paralysed arm, and when we remember that damage to the central nervous system, whether experimental or clinical (it is the commonest cause of hyperpyrexia in man), frequently causes such a high temperature that we must suppose the production of heat to be increased, the observa

tions I quote do lend strong support to the view that when in hemiplegia the temperature is raised in the paralysed axilla the increased quantity of heat in the paralysed arm is due to a greater production of heat in the paralysed than in the corresponding unparalysed limb. If this is so we have an instance in which a lesion that paralyses the motor function of muscle excites the thermogenetic, and thus we see that the functions are distinct.

D. *Temperature raised in fever.*—In any fever the general condition and temperature of different patients vary very much, and, therefore, single observations would be of little value. I have consequently made several observations on different patients in the following fevers, and if all the cases of any particular fever point in the same direction we shall probably be justified in drawing conclusions. I have always compared the observations made on a patient with a febrile temperature with those made on the same patient before he got up, but when his temperature was normal, or very nearly normal, unless his death prevented this.

I. *Typhoid fever* (see Table XI.).—The table shows that in all cases the amount of sweat secreted during the fever was small (from 2 to 3 milligrammes in ten minutes is the usual amount my boxes absorb from the abdomen of a healthy man) and less than when the temperature had fallen, therefore during the fever the loss of heat from evaporation was diminished. Also in every case except one the surface temperature rose less than the internal—in other words, the loss from radiation and conduction was not increased proportionately to the rise of internal temperature, and was therefore, relatively to the internal temperature, less during the fever. Thus, there is distinct evidence that in typhoid fever the loss of heat is relatively to the rise of temperature diminished, and this diminished loss no doubt helps to raise the internal temperature. Still, as the surface temperature always rose considerably, the actual loss by radiation and conduction must have increased during the fever, and probably the decreased secretion of sweat was not enough to counteract this. Therefore we may conclude that although certainly in typhoid fever the pyrexia is largely due to a lessened loss of heat, yet probably, too, the production is increased. Typhoid fever is remarkable in that, although it is a long-lasting disease with a high temperature, it has a low mortality; and these results suggest that one reason for this may be that the temperature is raised with the least expenditure of energy, for it is obviously more economical of energy to raise the temperature by diminishing the loss of heat than by increasing the production. Then, too, it is interesting to note that experience has shown that the best way to reduce pyrexia in typhoid fever is by sponging, that is by increasing the loss of heat. It is well known that the internal temperature of typhoid fever is irregular as convalescence approaches, and we see that the

same is true of the surface temperature (see Case 5, high readings on 5th and 6th) and sweat (same case, reading on 5th). In Case 7 it will be noticed that as the patient got worse the surface temperature approached the internal—that is to say, he was dissipating energy the faster.

II. *Pneumonia* (See Table XII.). All these cases, except the first, show that the excessive sweating which is associated with the crisis lasts some days after it, and the fourth case shows how enormous the sweating of the crisis may be. This sweating must aid in keeping down the temperature after the fever. In every case during the fever the secretion of sweat is less than when the temperature has fallen, but as then the secretion is still rather more than in healthy individuals and in typhoid fever patients whose temperature has fallen, probably the sweat secreted during fever is not much less than before the fever began. Therefore it appears that the diminution of the loss of heat owing to a diminution in the amount of sweat secreted plays but a small part in raising the temperature. In only two cases did the surface temperature rise less than the internal, and in two it rose more (this explains the hot skin of pneumonia), therefore often in pneumonia the loss by radiation and conduction during the fever must be enormous. As, therefore, in pneumonia the loss of heat is so increased, the rise of temperature is for the most part due to an increased production of heat.

III. *Erysipelas* (see Table XIII.).—In both these cases the sweat was increased during the fever, and the surface temperature rose more than the internal temperature, so the dissipation of heat by evaporation, conduction, and radiation must have been very much increased. Consequently, the rise of temperature must have been entirely due to an increased production of heat, and not at all to a diminution of the loss.

IV. *Suppuration* (see Table XIV. A).—Here the considerable amount of sweat secreted after the abscess was opened and the temperature had fallen appears to show that sweating helped to keep the temperature down. In the first case at least the quantity secreted during the fever was so small that the raised internal temperature may have been partly due to a diminished loss of heat from lessened evaporation. In both cases, too, there was a diminished loss from radiation and conduction, for the rise of surface temperature was less than that of the internal temperature, in fact, on one occasion, the surface temperature was actually lower during the fever than when the internal temperature had fallen, and that although there was no excessive evaporation of sweat to bring it down. We may conclude that in these two cases of suppuration the raised internal temperature was, in part at least, due to a diminution in the loss of heat.

TABLE X.—TEMPERATURE RAISED BY DAMAGE TO THE BRAIN.

Case.	Date.	Temperature in the axilla, paralysed side.	Deg. F.	Temperature in the axilla, non-paralysed side.	Deg. F.	Axillary difference on paralysed side.	Deg. F.	Surface temperature on paralysed forearm.	Deg. F.	Surface temperature on non-paralysed forearm.	Deg. F.	Surface difference on paralysed side.	Milligrammes of sweat on paralysed forearm in ten minutes.	Milligrammes of sweat on non-paralysed forearm in ten minutes.	Difference in milligrammes of sweat on paralysed forearm.	Remarks.
Man.—Right cerebral hemorrhage, left hemiplegia. Onset, July 11th, 1896.	July 13th, 1896 (morning)	100.8	Deg. F.	100	Deg. F.	+ 0.8	Deg. F.	92.8	Deg. F.	92.8	Deg. F.	0	41.1	21.2	+ 19.9	Increased sweat on paralysed side in both cases obvious to feel. The skin was gently wiped before observations; no vascular difference was visible.
		100.6	Deg. F.	100	Deg. F.	+ 0.6	Deg. F.	93.2	Deg. F.	93.2	Deg. F.	0	13.5	4.3	+ 8.2	
		97.8	Deg. F.	97.0	Deg. F.	+ 0.8	Deg. F.	93.6	Deg. F.	92.8	Deg. F.	+ 0.8	5.4	6.1	- 0.7	
Man.—Right cerebral hemorrhage, left hemiplegia. Onset, Aug. 8th, 1896.	Aug. 23rd, 1896	77.0	Deg. F.	96.6	Deg. F.	+ 0.4	Deg. F.	92.8	Deg. F.	91.8	Deg. F.	+ 1.0	8.1	4.3	+ 3.8	No vascular difference was ever visible. (In both patients the observations on the two sides were always simultaneous.)
		98.2	Deg. F.	98.0	Deg. F.	+ 0.2	Deg. F.	94.4	Deg. F.	93.8	Deg. F.	+ 0.6	8.3	5.9	+ 2.4	

TABLE XI.—TYPHOID FEVER.

Case.	Date.	Mouth temperature.	Abdominal surface temperature.	Mouth exceeded surface by—	Excess of mouth during fever.	Excess of surface during fever.	During fever surface rose more or less than mouth.	Milligrammes of sweat from abdomen in ten minutes.	Greater or less sweat during fever in milligrammes.	Remarks.
		Deg. F.	Deg. F.	Deg. F.	Deg. F.	Deg. F.	Deg. F.			
1. {	June 9th, 1896	102.0	95	7.0	—	—	—	0.7	—	}
	July 2nd, 1896	98.2	92	6.2	3.8	3.0	- 0.8	2.1	1.4	
2. {	June 9th, 1896	102.0	97.8	4.2	—	—	—	1.1	—	}
	July 2nd, 1896	98.0	93.2	4.8	4.0	4.6	+ 0.6	1.3	0.2	
3. {	Oct. 22nd, 1896	102.6	96.0	6.6	—	—	—	0	—	}
	Oct. 23rd, 1896	103.0	96.0	7.0	—	—	—	—	—	
	Nov. 3rd, 1896	99.4	94.8	4.6	3.6	1.2	2.4	3.0	3.0	
4. {	Oct. 22nd, 1896	103.0	97.2	5.8	—	—	—	1.4	—	}
	Oct. 23rd, 1896	102.8	97.5	5.3	—	—	—	0	—	
	Nov. 3rd, 1896	98.8	95.2	3.6	4.2	2.0	- 2.2	7.2	5.8	
5. {	Dec. 3rd, 1896	104.0	93.2	10.8	—	—	—	1.0	—	} A mild case. The first observation was on the eleventh day of the illness. The contrast has been made between this (because the fever was then at its height) and the last.
	Dec. 4th, 1896	102.4	93.2	9.2	—	—	—	1.0	—	
	Dec. 5th, 1896	100.6	95.0	5.6	—	—	—	7.0	—	
	Dec. 6th, 1896	102.2	100.4	1.8	—	—	—	0	—	
	Dec. 7th, 1896	99.0	91.4	7.6	—	—	—	0	—	
	Dec. 8th, 1896	99.8	93.2	6.6	—	—	—	1.0	—	
	Dec. 9th, 1896	98.4	91.4	7.0	—	—	—	1.5	—	
	Dec. 10th, 1896	99.4	93.2	6.2	—	—	—	2.5	—	
	Dec. 11th, 1896	98.4	91.4	7.0	5.6	1.8	- 3.8	3.0	2.0	
	April 10th, 1896	103.7	96.8	6.9	—	—	—	2.2	—	
6. {	April 14th, 1896	102.8	96.4	6.4	—	—	—	0.7	—	} Patient died from hæmorrhage.
	April 18th, 1896	103.0	96.6	6.4	—	—	—	1.2	—	
	May 2nd, 1896	104.0	96.8	7.2	—	—	—	1.3	—	
7. {	May 11th, 1896	105.6	101.3	4.3	—	—	—	0.9	—	} Patient died very soon after the last observation from intensity of disease.
	May 14th, 1896	102.3	99.2	3.1	—	—	—	1.9	—	

TABLE XII.—PNEUMONIA.

Case.	Date.	Mouth temperature.	Abdominal surface temperature.	Mouth exceeded surface by—	Excess of mouth during fever.	Excess of surface during fever.	During fever surface rose more or less than mouth.	Milligrammes of sweat from abdomen in ten minutes.	Greater or less sweat during fever in milligrammes.	Remarks
		Deg. F.	Deg. F.	Deg. F.	Deg. F.	Deg. F.	Deg. F.			
1. {	March 6th, 1896	104.2	97.6	6.6	—	—	—	1.8	—	} First observation taken immediately before the crisis.
	March 10th, 1896	99.6	92.6	7.0	4.6	5.0	+ 0.6	2.4	0.6	
2. {	April 30th, 1896	103.6	97.8	5.8	—	—	—	4.1	—	} Second observation taken a few days after the crisis.
	May 7th, 1896	98.8	93.0	5.8	4.8	4.8	0	5.9	1.8	
3. {	July 11th, 1896	103.8	96.8	7.0	—	—	—	2.1	—	} Second observation taken four days after the crisis.
	July 20th, 1896	98.0	95.0	3.0	5.8	1.8	- 4.0	5.6	3.5	
4. {	Nov. 29th, 1896	102.8	96.0	6.8	—	—	—	2.2	—	} Second observation taken just at the end of the crisis.
	Nov. 30th, 1896	98.0	92.2	5.8	—	—	—	40.0	—	
	Dec. 2nd, 1896	98.4	92.2	6.2	—	—	—	12.0	—	
	Dec. 3rd, 1896	98.0	92.2	5.8	—	—	—	13.0	—	
	Dec. 11th, 1896	98.0	93.0	4.8	4.8	3.0	- 1.8	5.5	3.3	
5. {	Dec. 10th, 1896	104.0	100.4	3.6	—	—	—	3.5	—	} Second observation taken a few days after the crisis.
	Dec. 17th, 1896	98.0	92.2	5.8	6.0	8.2	+ 2.2	5.0	1.5	

TABLE XIII.—ERYSIPELAS.

Case.	Date.	Mouth temperature.	Abdominal surface temperature.	Mouth exceeded surface by—	Excess of mouth during fever.	Excess of surface during fever.	During fever surface rose more or less than mouth.	Milligrammes of sweat from abdomen in ten minutes.	Greater or less sweat during fever in milligrammes.	Remarks.
1. {	Aug. 18th, 1896	Deg. F. 102·8	Deg. F. 101·4	Deg. F. 1·4	Deg. F. —	Deg. F. —	Deg. F. —	4·2	—	—
	Aug. 19th, 1896	102·4	100·4	2·0	—	—	—	3·9	—	—
	Aug. 22nd, 1896	98·6	94·6	2·0	4·2	6·8	+ 2·6	3·2	+ 1·0	—
2. {	June 30th, 1896	100·2	96·8	3·4	—	—	—	3·2	—	—
	July 2nd, 1896	97·0	92·8	4·2	3·2	4·0	+ 0·8	1·4	+ 1·8	—

TABLE XIV. A — SUPPURATION.

Case.	Date.	Mouth temperature.	Abdominal surface temperature.	Mouth exceeded surface by	Excess of mouth during fever.	Excess of surface during fever.	During fever surface rose more or less than mouth.	Milligrammes of sweat from abdomen in ten minutes.	Greater or less sweat during fever in milligrammes.	Remarks.
1. {	April 30th, 1896	Deg. F. 103·6	Deg. F. 95·5	Deg. F. 8·1	Deg. F. —	Deg. F. —	Deg. F. —	0·3	—	Abscess due to appendicitis. Opened May 9th, 1896.
	May 2nd, 1896	103·8	98·6	5·2	—	—	—	0·2	—	
	May 11th, 1896	100·4	96·3	3·6	—	—	—	5·9	—	
	Compared with first observation	3·2	- 1·3	- 4·5	—	5·6	—
	Compared with second observation	3·4	1·8	- 1·6	—	5·7	—
2. {	March 9th, 1896	104·0	94·0	8·0	—	—	—	3·0	—	Abscess connected with perforating ulcer. Opened March 10th, 1896.
	March 12th, 1896	99·6	91·0	8·6	4·4	3·0	- 1·4	5·0	2·0	

V. *Tubercle* (see Table XIV. AA).—I have made several observations on patients who were suffering from tubercle. Although the temperature fluctuates considerably they are always suffering from their disease, and therefore it is very difficult to obtain a normal standard. Consequently, I do not

TABLE XIV. AA.—TUBERCLE.

Case.	Date.	Mouth temperature.	Surface temperature.	Mouth exceeded surface by—	Milligrammes of sweat from abdomen in ten minutes.	Remarks.
1 {	May 20th, 1896	103.0	96.8	6.2	9.3	} Phthisis; bad case.
	May 31st, 1896	103.8	98.0	5.8	5.1	
	June 2nd, 1896	98.2	95.8	2.4	6.2	
2 {	March 16th, 1896 (4 P.M.)	104.0	96.4	7.6	30.0	} Phthisis; bad case. Sweat observations taken in palm, but even for the palm the amount is very great.
	March 17th, 1896 (1 A.M.)	102.6	95.9	6.7	9.2	
	March 17th, 1896 (5 P.M.)	104.0	96.8	7.2	30.6	
	March 18th, 1896 (1 A.M.)	103.8	95.2	8.6	28.6	
	March 18th, 1896	104.2	94.9	9.3	12.8	
3 {	Nov. 23rd, 1896	99.0	97.0	2.0	—	} Phthisis.
	Nov. 23rd, 1896	99.2	97.0	2.2	5.0	
	Nov. 23rd, 1896	98.0	94.2	3.8	8.0	
4 {	Nov. 26th, 1896	100.5	95.0	5.5	4.0	} Phthisis.
	Nov. 30th, 1896	99.0	91.4	7.6	8.0	
5 {	Nov. 26th, 1896	100.8	92.2	8.6	3.0	} Phthisis.
	Nov. 28th, 1896	98.8	92.2	5.8	9.0	
	Dec. 1st, 1896	99.2	92.2	7.0	3.0	
6 {	June 10th, 1896	104.0	100.4	3.6	1.9	} General Tuberculosis.
	June 11th, 1896	104.5	99.5	5.0	1.1	
7	Oct. 28th, 1896	101.2	97.6	3.6	3.3	} General Tuberculosis.
8	Oct. 28th, 1896	101.4	97.8	3.6	4.0	} General Tuberculosis.

think the figures teach much about the process of this fever. You will notice, however, that the amount of sweat secreted is large even when the temperature is low, so that no doubt the increased secretion of sweat is often the cause of the fall of temperature. It is interesting to notice that, on the whole, the cases of general tuberculosis secreted less sweat

than those of phthisis. In both forms of disease the surface temperature is, as a rule, low; this may be due to the large amount of sweat secreted. As the evaporation of this sweat must lead to a considerable loss of heat it is probable that in tubercle the production of heat is, as a rule, increased.

It appears from these observations that in some fevers the pyrexia is, in part at least, due to a diminished loss of heat, in others this is of but slight importance, and then the production of heat is very great; and this result goes to prove the truth of the suggestion I made earlier in these lectures—namely, that the processes which lead to a rise in temperature are different in different fevers. We have also incidentally learned much about the surface temperature and the secretion of sweat in the fevers we have considered.

TABLE XIV. B

Time.	Volume of arm.	Temp. (Deg. C.).
10.50	100	36.8
10.55	100	36.9
11.15	97	36.8
11.20	95	36.8
11.30	88	36.9
12.0	85	36.8
12.15	80	36.8
12.30	80	36.8
1.0	70	36.8
1.15	65	37.0
1.30	60	37.3 (slight shiver)
1.35	57	37.5
1.50	54	37.7
2.0	53	38.3
2.10	53	38.5
2.20	51	39.0
2.25	50	39.2
2.30	50	39.5
2.40	49	39.6

Before leaving this subject I should like to draw your attention to some interesting figures obtained from a case of leucocythæmia. There was one white corpuscle to every ten red. The hæmoglobin was reduced to 17 per cent. of the normal, and the red corpuscles to 24 per cent. An observation gave the following result. The temperature of the mouth was 102.2°. The surface temperature at the umbilicus was 102.2°. The amount of sweat secreted in ten minutes was 1.2 milligramme. There are two points of interest here. First we have the high surface temperature with very little sweat;

probably it would be impossible to have so high a surface temperature if there were much sweat, for the evaporation of the sweat would reduce it. Secondly, as the surface temperature was so high the loss by radiation and conduction must have been excessive, so the production of heat must have been very great, and therefore even the small amount of hæmoglobin and the plasma carried between them enough oxygen for the metabolism necessary for this increased production. My best thanks are due to my house physicians, Dr. A. Salter and Mr. C. J. Harnett, for much help in these investigations. I have many observations on other fevers which I hope to publish subsequently.

Maragliano has published some observations which do not bear on the question of the production of heat, but they at any rate show that in some fevers the temperature depends very much upon the state of the cutaneous circulation—that is to say, upon the loss from radiation and conduction. He⁴ applied the plethysmograph to the arm of fever patients after experiments on healthy men, and, in the fevers upon which he experimented, he found that as the internal temperature rose the volume of the arm diminished, and as the volume of the arm is chiefly dependent upon the flow of blood through the vessels of the skin, it follows that this was diminished; in other words, less heat was lost by radiation and conduction when the internal temperature rose. The table I show you gives the results obtained by observing a man suffering from malaria (see Table XIV. B).

It will be observed that the contraction of the vessels preceded the rise of internal temperature. This is very strongly suggestive that it was the cause of it, and in the following table (I have only quoted the part of it which refers to the rise of the volume of the arm) (Table XIV. C) which gives results obtained from a young man suffering from ague, we also see that the vessels begin to dilate before the internal temperature begins to fall—a fact which also strongly suggests that the fall of temperature was due to the increased vascular cutaneous dilatation.

I should now like to refer to some observations which Dr. Archibald Garrod and I made upon each other with the object of finding out how healthy individuals varied their loss of heat under different circumstances. Table XV. shows the results of six pairs of observations made upon us, each pair being made at the same time. The first five pairs were all made after dinner in the evening. It will be noticed that in these five pairs the temperature of the mouth of both of us was almost the same, but that four times out of the five my surface temperature was higher than his—on two occasions (the second and third) as much as 3·6° F. A possible explanation for the fact that on the fourth occasion my surface temperature was lower than his is that we made the observations in his house, which is about 200 yards from

⁴ Das Verhalten der Blutgefäße im Fieber und bei Antipyrese, Zeitschrift für Klinische Medizin, Band 14, 1888.

mine, and on the evening on which this observation was made I strolled to his house after dinner while there was a cold north-east wind blowing. On four out of the five occasions I sweated more than he did. The whole amount I perspired during the five observations was 15·3 milligrammes, but his

TABLE XIV. C.—YOUNG MAN WITH AGUE.

Time.	Volume of arm.	Temp. (Deg. C.).
11.0	60	39·9
11.10	62	40·3
11.30	60	40·6
11.45	68	40·6
12.0	76	40·6
12.15	74	40·6
12.30	78	40·5
12.45	82	40·3
1.0	82	40·4
1.15	90	40·2
1.30	96	40·0
2.0	108	40·0
2.30	120	40·0
3.0	126	39·8
3.30	133	39·7
4.0	138	39·5
4.30	143	39·4
5.0	149	38·9

total amount was only 11·1, so that I perspired 38 per cent. more than he did. As, therefore, my surface temperature was higher and the amount of sweat that I secreted was greater I lost heat from radiation, conduction, and evaporation faster than he, and therefore my production per kilogramme was greater than his. We consequently learn that even healthy individuals vary much in their production and loss of heat. The last pair of observations is of little value, as the temperature of our baths was not the same. I have given in the table the temperature of the air, taken with both a wet and dry bulb thermometer. The air was driest on April 11th, on which day I sweated most, but this was not the day that Dr. Garrod sweated most; and on the next driest day I sweated less than on any other, so as far as these few observations go they do not show any relation between the humidity of the air and the amount of sweat secreted.

It is well known that muscular contraction is accompanied by a rise of temperature; therefore, were it

TABLE XV.

Date.	Time.	Temperature of air.		Observations on Dr. Garrod.			Observations on self.			Remarks.
		Dry bulb thermometer.	Wet bulb thermometer.	Mouth temperature.	Temperature of surface of abdomen.	Milligrammes of sweat in ten minutes from abdomen.	Mouth temperature.	Temperature of surface of abdomen.	Milligrammes of sweat in ten minutes from abdomen.	
April 6th, 1896.	9.30 p.m.	68.5	60.0	Deg. F. 97.8	Deg. F. 91.8	2.8	Deg. F. 98.2	Deg. F. 92.7	2.8	1 hour after dinner.
April 7th, 1896.	9 p.m.	67.0	61.8	98.5	89.6	2.1	98.4	93.2	3.0	1½ hours after dinner.
April 11th, 1896.	9.15 p.m.	67.8	57.2	98.6	89.6	2.3	98.4	93.2	3.6	1½ hours after dinner.
April 13th, 1896.	9 p.m.	61.8	53.1	98.5	92.2	2.0	98.3	90.4	2.5	1½ hours after dinner.
April 14th, 1896.	10.15 p.m.	63.5	58.0	98.5	91.3	1.9	98.3	91.7	3.4	1½ hours after dinner.
April 15th, 1896.	9.30 a.m.	60.0	54.0	97.5	86.4	2.8	98.6	93.0	2.8	1½ hours after breakfast; bath before breakfast.

TABLE XVI.—EFFECT OF EXERCISE ON DR. GARROD.

Date.	Mouth temperature before exercise.	Mouth temperature after exercise.	Variation.	Abdominal surface temperature before exercise.	Abdominal surface temperature after exercise.	Variation.	Milligrammes of sweat in 10 minutes from abdomen before exercise.	Milligrammes of sweat in 10 minutes from abdomen after exercise.	Variation.	Form of exercise.
	Deg. F.	Deg. F.	Deg. F.	Deg. F.	Deg. F.	Deg. F.				
April 19th, 1896.	97.8	98.6	+ 0.8	87.0	92.7	+ 5.7	2.4	4.4	+ 2.0	3½ miles fast walking.
May 10th, 1896.	97.7	98.5	+ 0.8	89.6	92.2	+ 2.6	2.0	0.8	- 1.2	5 miles fast walking.
May 13th, 1896.	97.4	97.6	+ 0.2	87.0	94.5	+ 7.5	1.6	3.6	+ 2.0	{ 7½ miles bicycle ride in 1 hr. in hot sun.
May 20th, 1896.	97.4	97.8	+ 0.4	88.8	94.5	+ 5.7	1.9	4.3	+ 2.4	{ 6 miles bicycle ride in 50 minutes.
June 13th, 1896.	97.4	98.5	+ 1.1	89.0	92.75	+ 3.75	2.5	19.2	+ 16.7	{ 8 miles bicycle ride in very hot sun.
Oct. 11th, 1896.	97.8	96.8	- 1.0	89.0	91.4	+ 2.4	1.8	1.2	- 0.6	{ 17 miles bicycle ride in a very cold N.E. wind.

TABLE XVII.—EFFECT OF EXERCISE ON SELF.

Date.	Mouth temperature before exercise.	Mouth temperature after exercise.	Variation.	Abdominal surface temperature before exercise.	Abdominal surface temperature after exercise.	Deg. F.	Variation.	Milligrammes of sweat in 10 minutes from abdomen before exercise.	Milligrammes of sweat in 10 minutes from abdomen after exercise.	Variation.	Form of exercise.
April 19th, 1896.	Deg. F. 98.2	Deg. F. 98.4	Deg. F. + 0.2	Deg. F. 91.4	Deg. F. 91.1	Deg. F. - 0.3	Deg. F. - 0.3	3.0	9.3	+ 6.3	{ 3½ miles fast walking with Dr. G.
May 10th, 1896.	Deg. F. 98.2	Deg. F. 98.8	Deg. F. + 0.6	Deg. F. 94.1	Deg. F. 93.6	Deg. F. - 0.5	Deg. F. - 0.5	3.7	6.8	+ 3.1	{ 5 miles fast walk with Dr. G.
May 17th, 1896.	Deg. F. 98.4	Deg. F. 98.4	Deg. F. 0	Deg. F. 90.5	Deg. F. 91.4	Deg. F. + 0.9	Deg. F. + 0.9	2.4	21.9	+ 19.5	{ One hour's hard walk on a very hot day.
June 20th, 1896.	Deg. F. 98.0	Deg. F. 98.2	Deg. F. + 0.2	Deg. F. 93.5	Deg. F. 92.6	Deg. F. - 0.9	Deg. F. - 0.9	3.3	16.0	+ 12.7	{ One hour's hard walk, but in a strong wind.
Oct. 11th, 1896.	Deg. F. 98.2	Deg. F. 97.4	Deg. F. - 0.8	Deg. F. 89.8	Deg. F. 89.5	Deg. F. - 0.3	Deg. F. - 0.3	0.5	1.4	+ 0.9	{ 17 miles bicycle ride in a very cold N.E. wind with Dr. G.
Oct. 20th, 1896.	Deg. F. 98.2	Deg. F. 98.2	Deg. F. 0	Deg. F. 89.5	Deg. F. 88.6	Deg. F. - 0.9	Deg. F. - 0.9	0.5	0.3	- 0.2	{ 14 miles bicycle ride in a very dry cold wind.

not that the loss of heat is increased during exercise the temperature would always rise. In fact, often the increased loss does not compensate for the increased production, and so the temperature does rise. Many references to this subject are given by Pembrey.⁵ Jurgensen found that the work involved in sawing wood for six hours raises the temperature of a healthy man 1.2° C. above normal. Davy showed that walking for two or three hours raised the temperature of the urine 0.8° C. Clifford Allbutt found that Alpine climbing raised the temperature of the mouth half a degree, and Liebermeister and Hoffman found their axillary temperature raised by the exertion both of coming up and going down a mountain. Hobday, too, has taken the rectal temperature of omnibus horses, and he finds that it is raised about 2° C. by hard work. Dr. Garrod and I thought, therefore, it would be of interest to make a series of observations on the effect of exercise on each other (see Tables XVI. and XVII.). It will be seen that a bicycle ride of seventeen miles in a high, dry, cold wind reduced the internal temperature of Dr. Garrod by 1.0, and my own by 0.8 of a degree. I do not think this can have been due to the inhalation of cold air cooling the mouth, for we did not take the temperature of the mouth until we had been in the house for twenty minutes after the ride, and it must have been due to the rapid loss of heat caused by our going quickly through the high, dry, cold wind. With the exception of this bicycle ride it will be seen that exercise always raised Dr. Garrod's internal temperature and that mine was either unaltered or raised, but that mine was, on the whole, much less affected than his. There are other interesting points of contrast between us. Dr. Garrod's surface temperature was always considerably raised by exercise, while mine was usually slightly diminished. On the other hand, he sweated but little in comparison with me, for his average increased amount of sweat was 3.5 milligrammes, while mine was 7.05. The difference is really greater than this, for I took two bicycle rides in a cold, dry wind to his one, and in a very dry wind the sweat evaporates fast, and consequently not much is secreted when the observation is taken. Apparently, therefore, we are different in our methods of accommodating the loss of heat to the increased production due to the muscular exercise; he chiefly increased his radiating and conducting power; I chiefly increased my loss by evaporation. We have therefore a demonstrated proof that different people accommodate differently. These tables, too, show strikingly what Table XV. has already shown—namely, that when at rest my surface temperature is always higher than Dr. Garrod's, and that I perspire more than he does; in other words, I lose heat faster and therefore must produce more calories per kilogramme. As in fever, so here the data are not sufficient for us to say how many calories of heat the muscular exercise causes to be produced—we can

⁵ Op cit.

only say that it must at least have been more than a certain number, for instance, my weight without my clothes is 61 kilogrammes; supposing the effect of exercise was to raise my temperature 0.5° C., and the loss by radiation, conduction, and evaporation were all increased, then I, as soon as when taking exercise I had raised my temperature the half a degree Centigrade, must have produced at least more than an additional 30.5 kilogramme Centigrade calories, as my specific heat is nearly that of water.

LECTURE III.¹

MR. PRESIDENT AND GENTLEMEN,—We now pass on to the second method which has been used in the endeavour to find out whether or not in fever the production of heat is increased—namely, calorimetry. The difficulty of the subject is very great, for although many experimenters have worked at it, if any reliable results have been published they are few, and I can well understand this, for I have been working at calorimetry for the last six years and have not yet satisfied myself that a trustworthy instrument has been made.

The calorimeter, which has hitherto been most frequently employed for measuring the heat given off by animals, is the well-known water calorimeter. Such an instrument was described by Crawford in 1788; and after reading the account of his experiments I doubt whether any of his successors have taken more elaborate precautions to ensure the greatest attainable accuracy. Other experimenters who have used water calorimeters are Dulong, Despretz, Senator, Wood, Desplats, Evans, Hare, Ott, Carter, Reichert, and Kemp. One of the most recent patterns of water calorimeter is that used by Reichert. It consists of two concentric boxes of sheet metal, which are fastened together so that there is a space of about one and a half inches between them filled with water. In the inner box the animal is placed, there being a suitable opening through both boxes for this purpose; the opening has an air-tight door. The inner box has leading into it two tubes—one for the entrance of air and the other for its exit. The outer box has a hole in it, through which passes a stirrer to stir the water between the two metal boxes, and another in which is fixed a thermometer to take the temperature of the water. The whole apparatus is surrounded by a thick packing of wool, feathers, or some other non-conductor, so that it is protected as far as possible from the effects of variations in the external temperature. The instrument is standardised before it is used for experiments on animals. This is done by burning in it enough of either hydrogen or alcohol to raise the temperature of the water 1°. It is known how many calories of heat are set free in the combustion of this quantity of hydrogen or alcohol, and therefore it is known that this number of calories is always given off to the instrument when the temperature of the water in it rises 1°. The temperature of the air entering and that of the air leaving the calorimeter is taken, and so any heat given off by the animal and expended in warming

¹ Delivered on June 24th.

the air is estimated. Lastly, the moisture given off by the animal is determined, so that the heat expended in volatilising its aqueous vapour can easily be calculated. All water calorimeters are unreliable, chiefly because, firstly, as I have often found, even with the most careful mixing, it is impossible to get a large mass of water to a uniform temperature, and a slight error as to temperature means an enormous error in the result of the experiment. Secondly, water calorimeters act very slowly. For instance, in some of Senator's experiments at the end of an hour the temperature of the water had only risen 0.2° C., and after this the further rise was trifling. Many observers have not used water calorimeters. In 1780 Lavoisier and Laplace used an ice calorimeter, and Dr. Marcet showed one not long ago at the Physiological Society, but I cannot criticise it as he has not yet published an account of it.

In 1849 Scharling used a form of air calorimeter. Vogel and Hirn each employed instruments very like Scharling's. Rosenthal described an air calorimeter in 1878 and Richet published an account of an air calorimeter in 1885. This was employed by Langlois in 1887, and Mosso used a very similar instrument in 1890. Sapalski and Klebs also used an air calorimeter. The following objections can be urged against all these calorimeters: 1. The calorimeters which have been previously standardised are faulty, for the method employed to standardise is open to considerable sources of error. Thus Richet in standardising his got figures varying from 66 to 91 from which to strike an average, and Langlois obtained figures varying from 59 to 74; and I think I shall be able to show that even where the figures are apparently more satisfactory they are not really of value if the instrument is to be used for animals. 2. Many conditions may not be the same during the standardising as during subsequent experiments. 3. All non-differential calorimeters are open to serious sources of error from the varying influence of the external air in abstracting heat from the instrument. Some experimenters have tried to allow for these and other errors (e.g., that due to variations of barometric pressure), but the correction is a very large percentage of the whole amount of heat produced. 4. In many calorimeters the ventilation is quite inadequate. 5. In some, as Richet's, if for any period during an experiment the production of heat decreases, this decrease is not measured by the instrument.

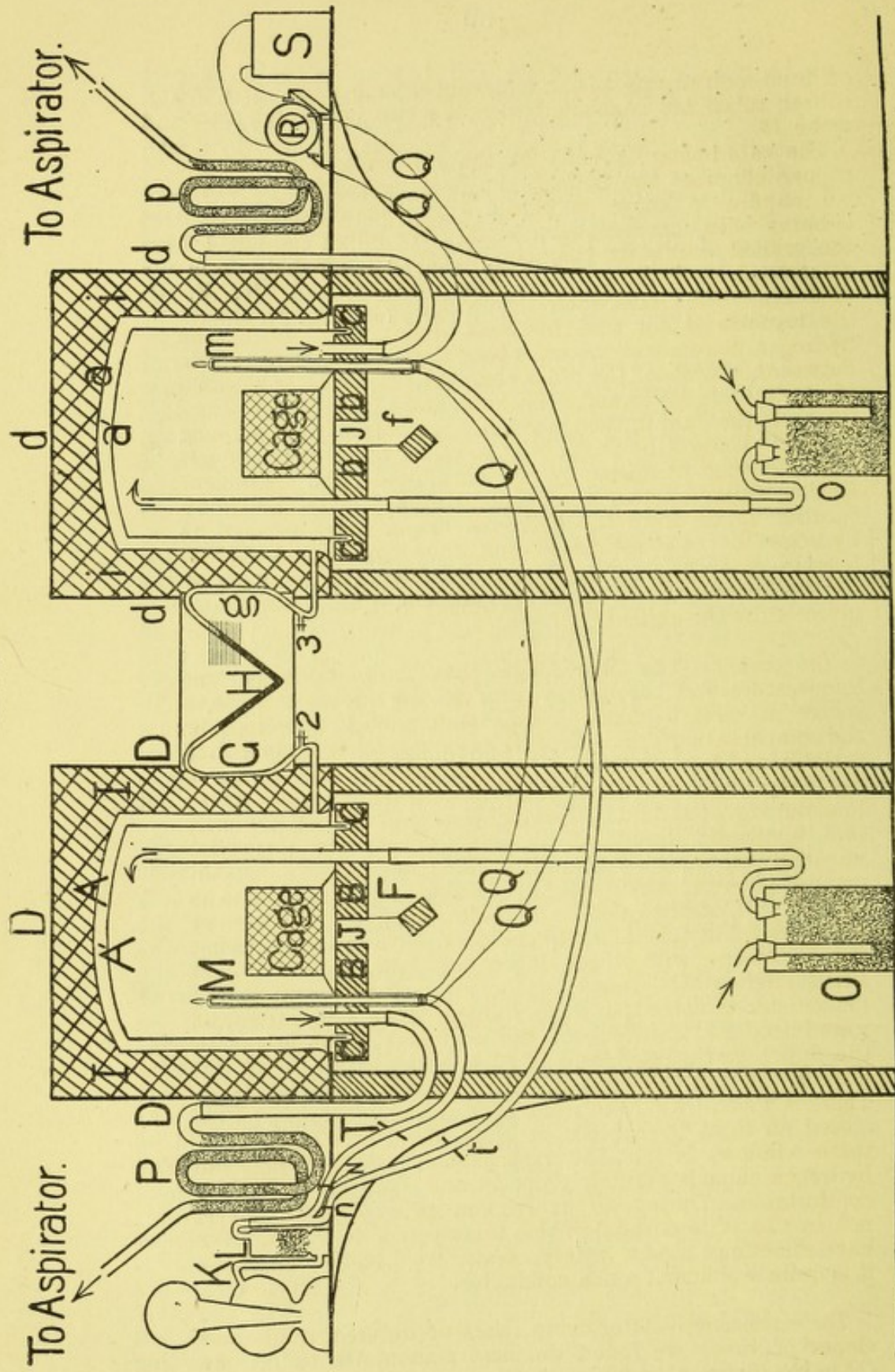
In 1886 D'Arsonval gave an account of several calorimeters, including his differential air calorimeter, which presents evident advantages over those described up to this date. My own apparatus embodies D'Arsonval's principle, but chiefly differs from his differential instrument in that there is a source of heat in both chambers of the calorimeter. Since the publication of this paper by D'Arsonval, and since I began to work at calorimetry, other calorimeters, for the most part modifications of D'Arsonval's differential instrument, have been described by Rosenthal, Ansiaux, and Rubner and his pupils. Calorimeters such as those

described by Liebermeister and Leyden, in which a part only of the body is inserted, are obviously unreliable, and so are the attempts made by Liebermeister, Kernig, and Hattwig to estimate the amount of heat produced by a man by immersing him in a water bath.

As differential air calorimeters have been most used, and have appeared to most observers to hold out the greatest promise of utility, I will describe in detail the one I have made. In making it I have derived much help from my friends, Dr. Haldane, Dr. Washbourn, and Mr. F. G. Hopkins. It consists of several parts (see Fig. 1).

The copper chambers.—These are two precisely similar cylindrical chambers made of thin sheet-copper and provided with convex roofs. The inside height of each is 18 in., and the inside diameter is the same. Each chamber has two walls (see diagram—A, A' and a, a'), between which is an air space $1\frac{1}{2}$ in. across and closed at the bottom by copper. Each chamber is by means of flanges turned out from its outer wall, A, a, firmly screwed on to a strong wooden table which stands on four wooden legs that are fixed to the floor of the laboratory. These legs are about 5 ft. high, so that it is easy with a little stooping to pass under them and open and shut the floor of the chambers. The floor of each chamber is a thick wooden disc (B, b) covered on its upper surface with copper. It is made of several layers of hard, well-seasoned wood so arranged that it does not warp under variations of temperature and moisture. These two floors are similar in all respects. Each disc has on its upper surface and near its circumference a deep trough (C, c) cut in it all round. The inner wall A' a' of the copper chambers is prolonged down into the trough. The trough C, c, in each disc is filled with resin ointment, in which, when the disc is pushed up as far as it will go, the prolongation downwards of the inner wall of the copper chamber is embedded, the chamber being thus closed air-tight. Resin ointment was chosen after many trials of various substances as being the best for rendering the chamber air-tight. Many varieties of screws were tried for keeping the discs in position, but we found that if a deep trough with plenty of resin ointment is used the chambers would keep shut absolutely air-tight for an indefinite time if the discs were kept in place against the wooden casing of the chambers by a simple button. It is very necessary that the parts of the instrument should be so arranged that the bottom of the trough does not, when the disc is pushed home, touch the prolongation of the copper down into the trough, and that the disc itself presses against the wooden table, and not against the copper air-tight space, for as the copper of which this is made is thin any pressure on it is liable to make the air-tight joints of the air-space between the outer and inner copper walls of each chamber give, and if they are not absolutely air-tight the instrument is quite useless. Leading

FIG. 1



off from each air-space is an indiarubber tube, G, g. The two rubber tubes are connected with the two limbs of a manometer H.

The calorimeter is used in the following way. In one copper chamber the animal, the heat production of which we require to know, is placed. In the other hydrogen is burnt, both chambers being shut. The heat given off from the animal warms its chamber, and thus increases the pressure of the air in the air-space between the two copper walls of its chamber. This would lead to movement of the fluid in the manometer but that the heat given off by burning the hydrogen increases at the same time the pressure in the space between the walls of the other chamber. This latter increase of pressure tends to make the fluid move in the other direction. If the fluid in the manometer is stationary the amount of heat given off by the animal is, other things being equal, equal to that produced by the burning of the hydrogen. During an experiment the manometer is kept stationary by turning up or down the hydrogen flame. The amount of hydrogen burnt is estimated, and knowing the heat of combustion of hydrogen we can calculate the calories produced by the quantity used in the experiment, which equal those given off by the animal.

The casing.—The knowledge that fluctuations in the temperature and barometric pressure are a most important source of error in many air calorimeters led to our adopting the compensating principle of D'Arsonval, for it is clear that variations of temperature and barometric pressure in the air of the laboratory would affect both air spaces equally and, therefore, not move the fluid in the manometer. We found, however, that temporary draughts, &c., were apt to act somewhat unequally on the two chambers, and thus cause a certain amount of error, which might in extreme cases amount to as much as 0.5 calories per hour. After very many trials we discovered that this difficulty could be obviated by covering the chambers with three layers of felt each an inch thick. When this was done the level of the fluid in the manometer remained stationary unless some source of heat were introduced into one of the chambers. The felt is in the figure marked I, i, and is of the kind used for refrigerators. It is all covered in with the wooden casing D, d. There is a small window in the floor of each chamber. It is closed air-tight by a piece of glass, J, j. The object of these windows is that the experimenter may see that the hydrogen flame is burning properly and that the animal is comfortable. During an experiment when the window is not in use it is covered with a thick pad of felt, F, f. We have sometimes used a variety of slag wool instead of felt—it is quite as efficient a non-conductor.

The manometer.—After many trials of different fluids and slopes of tubes we found the best manometer to be one (H in the diagram) in which the limbs are sloped at an angle

of 45° with the horizon. The bore of the tube is one tenth of an inch in diameter. It is filled with oil of erigeron, as the specific gravity of that is very low and it moves readily. Behind one limb of the manometer is a ruled scale. The lines are one-thirtieth of an inch apart and each is numbered. The scale is so placed that the lines on it are parallel with the upper surface of the fluid in the manometer. At the beginning of an experiment a note is made of the line which corresponds to the upper level of the fluid, and by turning the hydrogen up or down the fluid is kept on this line during the whole experiment. The openings 2, 3, which are kept clamped, on the manometer tube are useful; for if at any time the fluid in one limb has from any cause got much higher than that in the other, opening the clamps immediately brings the fluid in the two limbs to the same level.

The hydrogen.—The hydrogen is produced in a Kipp's apparatus, K, and is dried in the bottle L. It will be noticed that there is a hydrogen burner (M, m) in each copper chamber. A great advantage of this is that a control experiment can be done at any time, for if both copper chambers are shut air-tight, and hydrogen is burnt in each, one or other of the two flames being kept at such a height that the fluid in the manometer remains stationary, and it is then found that in the same time the same amount of hydrogen has been burnt in each chamber, it is evident that the instrument is not leaking. Some examples of this mode of control will be given immediately. Another reason for having a hydrogen burner in each copper chamber is that it is important for the fittings of the two chambers to be similar in all respects, so that those of one may not absorb more heat than those of the other. Therefore, also, there is in the hydrogen chamber a wire cage exactly similar to that used for the animal in the other chamber. The cages have a floor to catch the urine, and feet to raise them from the floor of the chamber and so prevent loss of heat by direct conduction from the animal to the floor of the chamber. The indiarubber tubes which conduct the hydrogen to the burners each pass under a screw clamp N, n, by means of which the size of the hydrogen flame can be very accurately adjusted. The amount of hydrogen burnt is estimated by determining the amount of water produced. This is effected by drawing a current of dry air into the calorimeter and estimating the moisture present in the outgoing air. The air entering the chambers is dried by means of Woulff's bottles (O, o), charged with pumice soaked in sulphuric acid. The air leaving the chambers is dried by being passed through the tubes P, p, which are filled with pumice soaked in sulphuric acid. Before the amount of moisture produced by burning the hydrogen in its chamber can be estimated the air in the chamber must be perfectly dry. To ensure this the chamber is shut up air-tight, the hydrogen not being lit, and then air which has been passed through a pumice and sulphuric acid bottle (O, o) is drawn through the chamber until a tube

containing pumice and sulphuric acid placed in the outgoing air-current no longer increases in weight. Six experiments of this nature showed that in order to completely empty all the moist air out of the chamber, and to replace it by dry air, 300 litres of dry air are required to be passed through. The following are the results of one of these experiments. The gains in weight of the pumice and sulphuric acid tubes in the out-going air-current after successive portions of dry air had been passed into the chamber are given.

Gain in weight after 92 litres of dry air were passed through	0.52 grms.
Further gain after 107 additional litres of dry air were passed through	0.17 "
" "	90 " "	0.05 "
" "	87 " "	0.00 "
" "	90 " "	0.00 "

Thus when 92 + 107 + 90 litres had been drawn through the air in the chamber was perfectly dry. The air is drawn through by means of a filter pump and measured with a wet gas meter, or a large graduated vat full of water may be used.

It is of great importance that the inner walls and floor of the chamber should present no hygroscopic surface. For this reason the floor is covered with copper. The employment of a painted surface gave endless trouble in the case of the first calorimeter in which the hydrogen method was employed.

Having dried the closed chamber the next thing is to light the hydrogen in it. This is effected by means of an electric spark. The wires Q, Q, proceeding from, and returning to, an induction coil R, connected with an accumulator S, are so arranged that a spark can be made to pass across the orifice of each hydrogen burner. The air in the chamber being dry a carefully weighed sulphuric acid and pumice tube is placed in the path of the outgoing current of air at P or p, as the case may be, according to which hydrogen burner is being used. The hydrogen is turned on; by passing the spark it is lit; and the aspiration through the chamber which had been stopped to put in the newly weighed tube is started. The moisture is absorbed by the tube at P or p, as the case may be. In an experiment with an animal, at the time that the hydrogen is lit, the animal in its cage is put in the other copper chamber, which is then shut up, and air is drawn through it to provide for the creature's respiration. In order to make the conditions similar air is drawn through the two chambers at an equal rate, which must be sufficiently rapid to prevent condensation of moisture. During an experiment the hydrogen is kept by means of the screw clamp N or n at such a height that the fluid in the manometer remains stationary. When the experiment has lasted as long as is desired the hydrogen is turned out and the animal is taken out of its chamber. But as the

air in the hydrogen chamber now contains moisture, and as we have already shown that to get rid of all the moisture in the chamber 300 litres of previously dried air must be drawn through it, this is done after the hydrogen is turned out. Then the increase in the weight of the tube at P or p will give the amount of moisture produced by the burning hydrogen. Suppose, for example, this were 4 grammes, then $\frac{1}{2}$ grammes = the weight of hydrogen burnt; and as the combustion of 1 gramme of hydrogen produces 34.2 kilogramme calories, $\frac{1}{2} \times 34.2$ equals the number of calories produced by the combustion of hydrogen in this experiment. This heat, however, is not all given up to the calorimeter, since the moisture produced is not allowed to condense inside the chamber. The heat of condensation of this moisture is $9 \times 0.59 = 5.3$ calories for each gramme of hydrogen. Hence the heat given up to the calorimeter is $34.2 - 5.3 = 28.9$ calories per gramme of hydrogen burnt, and this, in the instance we are supposing, multiplied by $\frac{1}{2}$ equals the heat given off by the animal. A calorie is taken to be the amount of heat necessary to raise one kilogramme of water through one degree Centigrade.

For turning out and lighting the hydrogen we found it convenient to have a spring clamp, T, t, on the hydrogen tubes, for then the hydrogen could be lit or turned out instantly; the screw clamp, N, n, is only used for adjusting the flame. It is absolutely necessary to show that the chamber and all the connexions are air-tight after the floor is pushed up at the beginning of an experiment. This is done by closing the inlet tubes to the bottles, O, o, and the hydrogen tubes, and then drawing a little air out of the apparatus and thus producing a negative pressure within, and then ascertaining—by means of the meter or a water manometer if the aspirating vat is used—whether this negative pressure is maintained. It will be noticed that the tube by which air enters the copper chamber is carried up to within an inch of the roof, while the orifice of the outlet tube is nearly flush with the floor. The object of this is to distribute the heat from the flame, and secure that by reflection from the roof the dry air entering the chamber shall be broken up as thoroughly as possible and so mixed with the moisture produced by the combustion of the hydrogen. A point we investigated was how much of the heat given off either by the burning hydrogen or by the animal was lost to the calorimeter, because it warmed the air drawn through the chambers. To determine this accurate thermometers were placed in the ingoing and outgoing currents of air, close to the copper chamber, by being inserted in an air-tight opening in the indiarubber tubes. It was found that after the animal had been in place, or the hydrogen had been burning an hour, the temperature of the outgoing air was never more than 0.4° C. higher than that of the ingoing. Now, usually 300 litres—that is to say, 400 grammes—of air were drawn through in an hour. The specific heat of air is 0.23; therefore, to warm 400 grammes of air through 0.4° C. would

take $0.4 \times 0.23 \times 0.4 = 0.037$ calories. But as a large rabbit gives off about nine calories an hour the heat given off by the animal or hydrogen flame, and not felt by the calorimeter because it is expended in warming the air, is only 0.4 per cent. of the total amount produced by the animal. As this amount is so small and is the same on the two sides of the calorimeter it may safely be neglected.

The instrument I have described to you is not quite the same as that which Dr. Haldane, Dr. Washbourn, and I described in the *Journal of Physiology*, but the principle is the same. The calorimeter of which I have now given an account is one that I made with Mr. Hopkins. It possesses several minor advantages over the instrument described in the *Journal of Physiology*. Its wooden casing is better than a casing of American cloth. The absence of pressure on the copper air space by the floor is very important, and it saves much trouble to dispense with the old arrangement for screwing the floor into position. It is much easier to ensure an air-tight space by having the window in the floor rather than in the walls of the air-tight space, and it is a great advantage to have the chambers so high from the ground that it is easy to pass under them. In the old instrument both chambers were fixed to one table, which made the whole very cumbersome and unwieldy, but as in the present instrument the manometer board is only on hooks the chambers with their casings are easily separated, the pumice tubes, the Kipp's apparatus, the induction coil, and the accumulator can easily be removed from the flaps on which they stand and the flaps let down. The long legs take off, and so the instrument can be easily moved. Lastly, we used a tube of pumice and sulphuric acid instead of a Woulff's bottle in the outgoing current, as that is easier to weigh.

Now I will bring forward some experiments to show that the instrument is correct in principle. In seven experiments both chambers were shut and shown to be air-tight. It was not necessary to empty them of the moist air they contained, for as both had been left open to the outside air before being shut the air in each contained the same amount of moisture. A sulphuric acid and pumice bottle was put in the path of the entering air and a weighed sulphuric acid and pumice tube was placed in the path of the air leaving each chamber. The hydrogen was simultaneously lit in both chambers, and the flame was kept in each at such a height that the fluid in the manometer was stationary. Aspiration at an equal rate through each chamber was carried on, and at the end of a given time, usually about an hour, both hydrogen flames were simultaneously turned out. Aspiration was then continued through both the chambers till 300 litres of air had been drawn through each after the hydrogen was turned out. By this means the equal amounts of moisture originally in each chamber and all the water produced by the burning hydrogen in each were absorbed. But as the fluid in the manometer had been kept stationary, or as nearly so as possible, it is clear that if the instrument is efficient equal amounts of

hydrogen should have been burnt—that is to say, equal amounts of water should have been produced. Therefore, if the increase of weight of the sulphuric acid and pumice tubes attached to the exit from each chamber was identical the instrument was working satisfactorily. The following table shows the results of these seven experiments (see Table XVIII.).

TABLE XVIII.

Grammes of water produced by hydrogen burning in west chamber.	Grammes of water produced by hydrogen burning in east chamber.	Error per cent.	No. of experiment.
3.98	3.83	3.7	1
4.4	4.32	1.8	2
3.1	3.15	1.5	3
2.04	2.01	1.9	4
1.52	1.52	—	5
3.27	3.37	2.9	6
3.0	3.06	1.9	7

West in excess three times—viz., 3.7, 1.8, and 1.9 per cent.

East in excess three times—viz., 1.5, 2.9, and 1.9 per cent.

West and east equal once.

Average error that the west is in excess 0.17 per cent.

It will be seen that on no occasion was the error greater than 3.7 per cent., and in five out of the seven it was under 2 per cent. The great advantage, as I have already insisted, of these controls in which hydrogen is burnt in both chambers is that as each chamber is fitted with a hydrogen burner a control can be done at any time in the course of a series of animal experiments. As far as I know, no large number of observations on animals have been carried out with such a calorimeter as I have described. I have only done, with the help of some friends, a few on rabbits and guinea-pigs. While the animal is being weighed and its temperature being taken the chamber in which the hydrogen is going to be burnt should be shut up air-tight, and then 300 litres of air, which has previously passed through a pumice and sulphuric acid bottle, should be drawn through it. When this is done the air in it will contain no moisture. A weighed sulphuric acid and pumice tube is then put in the outgoing current of air from the hydrogen chamber. The cage for the animal is then taken out of its chamber, the animal is put in it, and the cage is replaced. The chamber is then shut up, the hydrogen in the other chamber is lit simultaneously, and the flame is kept at such a height that the level of the fluid in the manometer is stationary. An equal quantity of air is drawn through each chamber, care being taken that enough is drawn through to prevent a deposit of moisture in the

chambers. At any given moment the animal may be taken out, but at the same moment the hydrogen must be turned out, the aspiration is continued through the hydrogen chamber for 300 litres, so that all the moisture produced by burning the hydrogen is collected in the exit sulphuric acid and pumice tube. The latter is then weighed, and from the increase of weight we can easily calculate the number of calories given off by the burning hydrogen to the calorimeter, which must, as the manometer has been kept steady, equal the number of calories given off by the animal to the calorimeter. The following are the details of an actual experiment:—

	Grms
Weight of sulphuric acid and pumice tube at exit of hydrogen chamber before experiment	3606·34
Weight of sulphuric acid and pumice tube at exit of hydrogen chamber after experiment	3607·92
	1·58
Water produced by hydrogen flame =	
Hydrogen burnt = $\frac{1·58}{9}$ = 0·176 grammes.	
Calories produced in the chamber = 28·9 × 0·176 = 5·08.	

The time the hydrogen was burning—that is to say, the time the animal was in its chamber of the calorimeter—was exactly one hour, so that the creature gave up to the calorimeter 5·08 calories per hour. The following are the results of four experiments made upon different days upon the same animal, a healthy brown male rabbit weighing 3080 grammes. The rectal temperature was always taken before and after the experiment (see Table XIX.).

TABLE XIX.

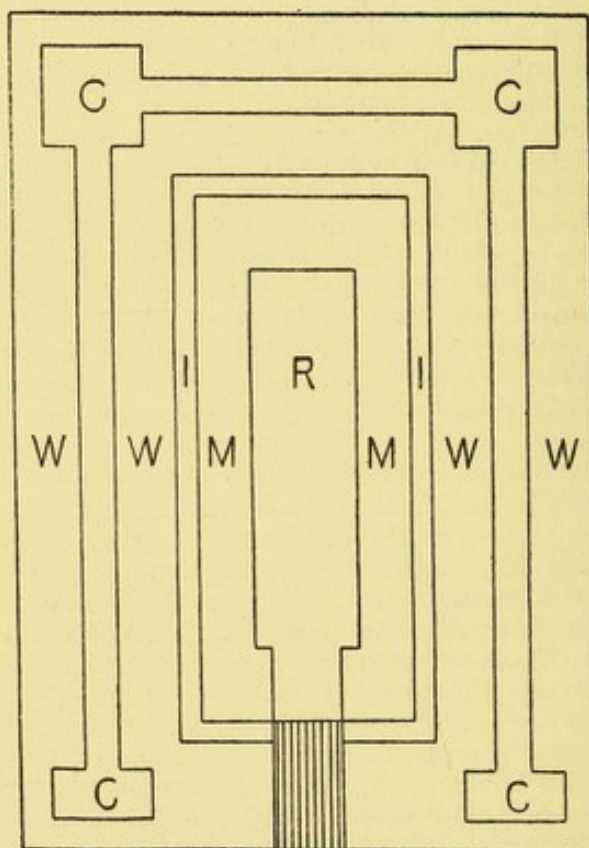
Calories given off per hour by the rabbit to the calorimeter.	Number of experiment.
7·37	2
6·89	4
6·64	1
5·08	3

Now these figures do not represent all the heat given off by the animal. I have already shown that the heat expended in warming the air drawn through the apparatus may be neglected, but that which is employed in volatilising the aqueous vapour given off from the animal is not included. The quantity of this aqueous vapour is determined by means of a pumice and sulphuric acid tube in the path of the air

coming from the exit of animal chamber. The heat required to evaporate a gramme of water at the temperature of the rabbit is a known constant (0.57 calorie), so that the heat expended by the animal in volatilising aqueous vapour can easily be obtained by multiplying 0.57 by the number of grammes of moisture given off by the animal. Thus when two guinea-pigs were in the calorimeter they gave off in an hour 1.74 grammes of moisture and $1.74 \times 0.57 = 0.99$, so that they gave off 0.99 calories by evaporation, which turned out to be nearly a fourth of what they gave off by radiation and conduction.

Rubner and Nebelthau have worked with very similar instruments to that which I have described. I show you a diagram of a section of Rubner's calorimeter (see Fig. 2).

FIG. 2.



It consists of a copper chamber R, in which the animal is placed; the chamber is closed by a non-conducting air-tight door. The copper chamber R is surrounded by an air space M, M, just as the copper chamber in the calorimeter I first described is surrounded by an air space; the air in this

space, M, M, is warmed by the animal, and as it expands it moves the dial of a registering apparatus, with which M, M, is connected by a tube. (This is not shown in the diagram.) I, I, is an air space closed on all sides by copper. The object of it is to surround the calorimeter with a good non-conductor, such as air. The whole is surrounded by a vessel containing a quantity of water, W, W, W. This also is to prevent the variations of external temperature from influencing the calorimeter. This mass of water is automatically kept at a constant temperature, for there is a gas flame under it, and if it gets too warm more cold water automatically flows in from a tap and replaces some warm water which automatically flows away. I need not bother you with the details of this arrangement. The registering apparatus is under the influence of variations in barometric pressure, and therefore there is a very irregularly shaped copper chamber, C, C, C, in the water W, W, W. This copper chamber is connected with a separate registering apparatus of its own and shows variations in the barometric pressure, and these are allowed for when calculating the heat given off by the animal by observing the registering apparatus connected with the air space, M, M. Of course, the animal chamber is ventilated. The apparatus is standardised by placing a spirally coiled tube in the animal chamber, letting warm water flow through the coil for a given time, and at the same time observing the movement of the registering dial connected with the air space around the animal chamber. The temperature of the water is taken before it enters and after it leaves the coil, and from these data it is easy to determine that the loss of so many calories of heat by the water corresponds to the movement of the hand of the registering dial through a certain distance. The ventilation of the animal chamber goes on during the experimental standardising of the instrument just as it would if an animal were in it, and the loss of heat from the water in the coil to the air drawn through is allowed for by taking the temperature of the air as it enters and as it leaves the chamber. It is impossible to take the temperature of the water immediately before it enters the coil or immediately it leaves it, for the tubes leading to and from the coil must pass through the water W, W, W, the air space I, and the air space M, before they can reach the coil. By preliminary experiments allowance is made for this. Now it appears to me that the disadvantages of this instrument are:—

1. If there is any error in the original standardising all the results obtained with the instrument are wrong.
2. As allowances are made in the original standardising there may well be some errors in it.
3. Any variation in the temperature of the water jacket will seriously affect the results, and it is a very difficult matter to keep a large mass of water at a constant temperature for a long time.
4. In every experiment all the conditions ought to be the same as during the standardising, but with this instrument this is impossible.
5. In every experiment allowance has to be made for

variations in the barometric pressure. It will hardly be disputed that an instrument which avoids all these possible fallacies is more likely to be accurate than one which does not, and therefore I cannot help thinking that the differential instrument I first described can be made to give more reliable results. Further, in general, the differential method is superior to that of primary standardising.

Nebelthau has worked with an instrument which is in principle the same as Rubner's, as it is an air calorimeter, and is standardised before it is used for an animal. It differs chiefly in that the chamber which shows the allowance to be made for variations of barometric pressure is quite detached from the animal chamber. We saw, when I was describing the calorimeter I have made, that if we want to calculate the whole heat produced by the animal we must include that which does not affect the calorimeter, but is employed in volatilising the water given off in the animal's breath. It is therefore necessary always to estimate the amount of aqueous vapour given off by the animal. This Nebelthau does with a hair hygrometer. I cannot help thinking that this is not so reliable a method as that of absorbing the water with sulphuric acid and pumice, and inasmuch as the heat lost in this way may be a fourth of that produced by the animal it is clear that it is of the utmost importance to estimate it accurately. Nebelthau has made a series of most laborious experiments. He has considered the influence of season, of time of day, of rapidity of ventilation, of moisture in the air, and of the size of the animal upon the heat production; I cannot for want of time stop now to consider the results he obtained, but must pass on to his experiments on fever. He used rabbits and produced fever in them by the injection of cultures of swine erysipelas. He estimated the heat production before and after the injection, and from the results obtained drew conclusions as to the production of heat in fever. He rightly points out the great importance of having the air entering the animal chamber of the same temperature during all the experiments on the same animal, for if it is not some of the variations in the creature's heat production may be due to the variation of the temperature of the air around it. If the air is not of the same temperature Nebelthau following Rubner makes a correction of 2.5 per cent. of the total heat lost for each degree of variation in the temperature. It is clear that if in any fever the rise of temperature were slight, the correction for variations of external temperature might bear a considerable ratio to the alteration in the loss of production of heat due to the fever, and, further, although no doubt the figure 2.5 per cent. was obtained from very careful experiments it is in the present state of our knowledge only an assumption that the figure is the same for all members of the same species. For these reasons I cannot help thinking that it would be better instead of making this correction to ensure that the temperature of the air, and, if possible, its humidity, were the same, at least during all experiments on

the same animal. Nebelthau's results are far too voluminous to give in full, but I show you two of them :—

TABLE XX.

Number of animal.	Weight.	Day.	Temperature of rabbit.	Calories.				
				Loss of heat by evaporation.	Loss by radiation and conduction.	Total.	Warmth lost per kilogramme per hour.	Per cent.
	Grms.		Deg. C.					
4	1703	1	39.0	17.75	91.93	109.68	2.683	100
	1625	2	41.7	19.17	109.29	128.46	3.294	122
	1545	3	40.5	18.08	113.64	131.72	3.544	132
7	2327	1	38.6	17.33	105.62	122.95	2.201	100
	2229	2	40.7	20.62	104.32	124.94	2.335	106
	2139	3	40.7	22.52	118.96	141.48	2.756	125

The first point to which he properly directs attention is that no air calorimeter really represents how much heat the animal produces. Air calorimeters are merely large air thermometers which are carefully protected from outside influences, so that any expansion of the air in them must be due to heat given off from the animal, and the amount of this heat lost by the animal is known either because the instrument has been previously standardised in calories by cooling water or because it can be estimated in calories from the hydrogen burnt in the opposite chamber. To obtain in calories the increased heat produced by the fevered animal in a given time (say, an hour) we must know its weight, the rise of its temperature, and its specific heat. (Nebelthau puts this at 0.8, which is, I think, a little too low; 0.95 is probably more accurate.) For instance, to take the first experiment I have quoted, the mean weight of the animal between the first and second days was the mean between 1703 grammes, its weight on the first day, and 1625 grammes, its weight on the second day; that is, 1.664 kilogrammes. Now, the temperature of an animal of a weight of 1.664 kilogrammes and of a specific heat of 0.95 rose 2.7°; therefore, if the loss of heat were unaltered, it must, to have raised its temperature 2.7°, have increased its heat production by $1.664 \times 2.7 \times 0.95 = 4.268$ calories; but we see from the table that from the first to the second day its heat loss to the instrument was increased from 2.683 to 3.294—that is, 0.611 calories per kilogramme of its body weight per hour. Therefore, its heat production

must have increased not only the 4 268 calories necessary to raise its temperature from 39.0° to 41.7° , but also enough to compensate for an increased loss in calories equal to 0.611 per kilogramme per hour.

Those of you who have followed me so far may be inclined to say that while it appears there are many sources of error to be guarded against if a calorimeter which has been previously standardised is used, yet if the differential calorimeter with hydrogen in one chamber and the animal in another be used, if the temperature and humidity of the air during all experiments on the same animal are the same, and if an accurate means of estimating moisture be employed, we ought to be able to find out from such a calorimeter whether or not the heat production is increased. I am afraid, however, that I must show you that the difficulties of the subject are not yet ended. The first difficulty we can see by looking at the table I have shown you of some figures obtained by Nebelthau. You will see that in the case of the first animal on the third day it was 80 grammes lighter and its temperature was 1.2° lower than on the second day. Either of these facts would constitute a reason why the creature should give off fewer calories on the third day than the second, but, as a matter of fact, it gave off more. Again, the second animal was on the third day 90 grammes lighter than on the second, and its temperature was the same on both days, yet when it was lighter it gave out considerably more calories than when it was heavier. Now all the instrument does is that it estimates the heat loss by radiation and conduction, because a mass of cooling water in losing a certain number of calories moved the indicator of the recording instrument through a given distance. But the water was losing heat uniformly, and it would be impossible for a mass of water which had decreased in weight and the temperature of which had fallen to give off more calories by radiation and conduction than it did before its weight had diminished or its temperature had fallen. Clearly, therefore, we are not comparing similar processes when we infer the amount of loss of heat from an animal because it moves the registering apparatus of an instrument standardised by cooling water. We cannot tell whether the first animal, for instance, was on the third day, by having altered its power of radiation and conduction, losing heat more rapidly, the production being the same or less, or losing it still more rapidly with an increased production. The falling temperature at first sight looks like a diminished production, but on the other hand, the increased radiating power may well indicate an increased production. It is true that when, as in the contrast between the first two days in each animal, the temperature rises and the loss also increases, the production of heat must be increased, but we cannot even then say whether the increased loss of heat is due solely to an increased production, the radiating power of the animal remaining the same, or an increase of both, but the increase

of the production being relatively greater, for in either case the number of calories lost would be greater and the temperature of the animal would rise. I am afraid this criticism applies equally to the calorimeter with double chambers, hydrogen being burnt in one and the animal placed in the other. The fallacy is essentially the same in both—namely, we are taking as a standard in both a source of heat (a hydrogen flame or a mass of cooling water) the loss by radiation and conduction from which is dependent solely upon the amount of heat in it, but the animal has the power of automatically altering its radiating and conducting power quite independently of the amount of heat in it, and also has the power of varying from time to time the rate of production of heat in it. These calorimeters measure the amount of heat lost; but as the animal can vary both the rate of production and rate of loss we cannot with them determine quantitatively the variation of production, and this is exactly the problem to be solved in fever. It is true, as I have shown, that we can get qualitative results, and often, as furry animals do not vary much in their powers of radiation and conduction, we can get rough quantitative results; but as man can by vascular dilatation and sweating vary his power of loss by radiation, conduction, and evaporation so enormously, we must be extremely careful how we apply results obtained from calorimetric experiments on furry animals to man.

The next difficulty I have to consider is that due to convection currents. When Mr. Hopkins and I were working at calorimetry we thought the instrument would be more easy to manage if it were so made that the top of it, rather than the bottom, took off, for then the weight of the lid would help to keep it well down in the grease trough. We therefore made such an instrument and suspended the animal from the lid. The hydrogen burners and the inlet and outlet tubes all came through the lid, and the hydrogen burners were so turned up as to make the flame turn upwards. Except for these alterations the instrument was precisely the same as I have already described, but of course it follows that there was no air-space at the top, for the lid contains no air-space; on the other hand, there was an air-space at the bottom. I should add that the position of the animal cages and hydrogen flames relative to the walls of the chamber was precisely the same when the lid was at the top as when it was at the bottom. We at once noticed that the instrument was not nearly so delicate when there was no air-space at the top as when there was one there. It was quite clear, therefore, that we had to deal with some factor, besides radiation and conduction, which influenced the instrument, and this could only have been convection currents. We next turned the instrument back again to its original position with the lids at the bottom, and we found that if a rabbit was in one chamber and no hydrogen burning in the other the manometer moved readily, and also if hydrogen was burnt in one chamber and there was no

animal or other source of heat in the other it also moved readily. Further, if hydrogen was burning in one chamber and a rabbit was placed in the other, and the hydrogen flame was kept at such a height that it exactly balanced the rabbit for a few minutes, during which no air current passed through either chamber, and then an equal current of air was drawn through each chamber, then the hydrogen had to be turned up at least 30 per cent. before a balance could be again obtained, and this although no condensation of water due to the burning hydrogen had taken place. This clearly shows that the convection currents from the rabbit and the hydrogen flame are affected unequally by an equal current of air passing through each chamber. It is certain, therefore, that convection currents are a very important factor, and that they are different from a minute point like a hydrogen flame, and a considerable surface like a rabbit's body; that this is so anyone can prove for himself by noticing the difference between the feeling of warmth he experiences when he holds his hand over a hydrogen flame and that which he experiences when he holds it the same distance over a rabbit, although the two about balance one another. The importance of convection is also seen by noticing how much hotter a hydrogen flame feels when the hand is held above it than it does when the hand is held equally far off it but at the side of it, although in both cases the radiant and conducted heat is the same, but the hand in the first case meets with more convection currents. This last observation corresponds to that in which we noticed that the instrument is so much more sensitive when the lid is at the bottom and the top is part of the air space than it is when the lid which contains no air space is at the top. When we first began making a calorimeter we tested its accuracy by putting a corked flask of cooling water of a temperature of from 40° to 50° C., but different at each experiment, on cork supports in one chamber and keeping the manometer steady by burning hydrogen in the other, both chambers being shut, and an equal air current drawn through each. When the water was taken out of the chamber its bulk was measured, and its bulk in litres at this temperature multiplied by $\frac{0.9}{1.00}$ gave its bulk at 4° C.—that is to say, its weight in grammes. Its weight in kilogrammes, multiplied by the number of degrees Centigrade through which the water had cooled, gave the number of calories given off by it, and this, together with the small quantity of heat given off by the cooling of the glass of the flask, represents approximately the heat given off by the water to its chamber of the calorimeter. To obtain an exact measure of this heat corrections would have to be made for the specific heat of water at from 40° to 45° and for the period (in all, about a minute) which elapsed between the time of reading the temperature of the flask and the time when it was placed in or removed from the chamber. The latter correction, which is small, and a correction for the loss of heat from the glass

of the flask were made, but the values given by recent observers for the specific heat of water at about 40° vary from 0.98 to 1.04, a difference of 6 per cent. We were, therefore, unable to make an exact comparison in absolute units between the number of calories given off by the flask and its water and those given off by the hydrogen flame. The following table shows the results of the six experiments (see Table XXI.).

TABLE XXI.

No. of experiment.	Number of calories produced by burning of hydrogen.	Number of calories given off by the flask.	Percentage excess on the part of the flask.
1	16.6	17.7	6.6
2	13.2	14.3	8.3
3	12.8	13.4	4.7
4	14.1	15.1	7.1
5	14.7	15.8	7.5
6	14.2	15.3	7.

It will be seen that there is a considerable error. At the time these experiments were made we were inclined to the opinion that the cause of this error lay in the fallacies just mentioned, but having since learned the importance of convection currents I cannot help thinking that a considerable part of the error was in each case due to the fact that the convection currents from the hydrogen flame and the water were different. I think there is no doubt, therefore, that because the convection currents from the hydrogen and animal are so different, because they are affected unequally by ventilation currents, and because so much of the effect of a source of heat on the calorimeter is the result of convection, no instrument is satisfactory which does not provide against the errors which may arise from unequal convection currents. I have already shown that the air drawn through the instrument is heated so little, and warmed air gives up its heat so slowly, that I do not think the difficulty would be satisfactorily met by taking the air, leaving the chamber through a spiral tube winding round in the air space connected with the manometer. The error due to convection is probably much less in Rubner's or Nebelthau's instrument than in mine, for it is likely that the convection currents from a spiral coil of warm water are much more like those from an animal than are those from a hydrogen flame, but it would make their instruments more trustworthy if they had been standardised with a coil of water the shape of the animal about to be experimented upon.

To sum up, I think we may conclude by saying:—1. No animal calorimeter that holds out any prospect of being

workable can give exactly the amount of heat produced by an animal, for when it shows an alteration in the number of calories lost it does not show what proportion of them have been lost because the creature's radiating power has been altered, and what proportion have been lost because the production has varied, but if we know the variation in the internal temperature of the animal, its weight and its specific heat, we can often say whether or not the production of heat is increased or diminished. In other words, we can get a qualitative but not an accurate quantitative result. 2. As in man alterations of loss of heat probably depend sometimes almost entirely on variation of production, and at other times almost entirely on variations in radiating and conducting power of the skin, we must be very careful in drawing conclusions from animals to man. 3. A differential instrument is very much better than one which has been standardised. 4. But the source of heat in the differential instrument must in shape resemble the animal which is to be observed, and the instrument, before the results it yields can be trusted, must be proved to register equally on both sides heat lost by radiation, conduction, and convection. I think it follows that no instrument has yet been devised which gives trustworthy results. I need hardly add that I say this with great regret, for I have for the last six years devoted all my spare time to calorimetry.

Before leaving this subject I should like to remind my hearers of two facts that are frequently lost sight of. The first is that we are too apt to talk of fever as though the process were the same whatever the cause of the fever, while really (as I have shown in the case of man) it is extremely probable that with all animals in some fevers the rise of temperature is chiefly due to variations in the production of heat, and in others it is chiefly due to variations in the loss, and any set of experiments only holds good for the particular animal and for the particular fever under consideration. Secondly, no calorimeter can register heat which is in the body converted into some other form of energy—e.g., motion. For instance, if we were to light a fire in a little locomotive and set it running up a spiral in our calorimeter, the instrument would only register such of the heat as is lost from the locomotive by radiation, conduction, and convection—it would not show that which was produced in the engine but at once converted into motion. If any heat in the living body is converted into motion we have no means of estimating it.

Many attempts have been made to make calorimetrical observations on parts of the human body, and as a rule the results are of little value; but lately Rumpel² has published some results which are so very interesting that it will be well to give an account of them. His experiments were all carried out on an arm placed in an air calorimeter made for it. From

² Ueber den Werth der Bekleidung und ihre Rolle bei der Wärmeregulation, Archiv für Hygiene, Band 9, S. 51.

what I have already said it follows that I do not think the results have more than a rough quantitative value. Rumpel shows, by putting first the clothed and then the unclothed arm in the calorimeter, that the loss of heat is greatly diminished by clothing, and he says that Rubner, working with a thermopile, has shown that if the radiation of heat from the naked skin be taken at 100, with a vest on it is 73; shirt and vest, 60; waistcoat, shirt, and vest, 46; and coat, waistcoat, shirt, and vest, 33; and if a guinea-pig's hair is cut off its loss of heat increases 33 per cent. In the first series of experiments a contrast was made between the arm clothed with dry clothes, that clothed with wet clothes, and the naked arm. Table XXII. shows the results.

TABLE XXII.

No. of experiment.	Naked arm gives off calories per hour.	Arm clothed with two layers of dry flannel gives off calories per hour.	Arm clothed with two layers of wet flannel gives off calories per hour.
1	7.92	4.25	—
2	7.41	—	7.45
3	8.39	—	7.96

These figures strikingly confirm the well-known fact that wet clothing is of no use in keeping the body warm. Indeed, it is worse than no clothing at all, for, in addition to the loss by radiation, there is the loss of heat from the evaporation of the water in the wet flannel, which in each of the above two cases was 15 calories. so that the total loss of heat was in the second experiment $7.45 + 15 = 22.45$; and in the third experiment it was $7.96 + 15 = 22.96$. The arm lost, therefore, when covered with wet clothing about three times as much heat as it would have done if it had been naked. The next experiments proved that the loss of heat in water is much greater than that in air at the same temperature (Table XXIII.).

TABLE XXIII.

Temperature of air or water Centigrade.	Calories lost per hour when the arm is naked in water.	Calories lost per hour when the arm is naked in air.	Calories lost per hour when the arm is clothed but in air.
Deg.			
11.5	157.0	12.5	8.4
16.2	103.0	10.9	7.6
20.9	81.0	7.8	5.6
24.7	54.0	7.9	5.0

If to the figures representing the loss of heat to the air we add the loss which is due to the evaporation of the perspiration it works out that at least eight times as much heat is lost in cold water as in air. As might be expected, cold water is worse than wet clothes. In one experiment in which the arm was clothed in wet clothes of a temperature of 20.6° C. the loss per hour was 29.8 calories, but in a bath of a temperature of 20.9° C. the loss per hour was 81 calories. The next table that I should like to quote shows in figures what is, I think, a well-acknowledged fact—namely, that the lower the temperature of the air the more valuable is clothing in saving heat (Table XXIV.). Another interesting table illus-

TABLE XXIV.

Temperature of air Centigrade.	Calories given off per hour from the unclothed arm.	Calories given off per hour from the clothed arm.	Difference.
Deg.			
6.6	14.27	10.69	3.58
10.6	12.84	8.64	4.20
15.8	11.05	7.69	3.36
20.8	7.79	5.59	2.20
23.6	4.92	4.23	0.69

trates very well that the addition of clothes diminishes the loss of heat (Table XXV.). It will be noticed that a linen

TABLE XXV.

Temperature of air C.	Naked arm lost calories per hour.	Arm clothed with wool vest and glove lost per hour.	Plus another wool vest.	Plus a linen vest.	Plus a coat.	Plus an overcoat.
Deg.						
15.5	9.71	8.73	—	—	—	—
16.7	9.30	—	8.18	—	—	—
15.9	10.0	—	—	8.18	—	—
16.8	10.2	—	—	—	6.89	—
15.2	—	—	—	—	—	6.81

vest is of no use in saving warmth. The last table that I shall quote illustrates that the same person may vary considerably at different times (Table XXVI.).

TABLE XXVI.

No.	Temperature of air Centigrade.	Naked arm gave off calories per hour.	Clothed arm gave off calories per hour.	Differ- ence.
	Deg.			
1. Frau G.	21·3	7·41	4·68	2·73
Ditto	20·3	6·57	3·97	2·60
2. Frau D.	19·2	6·54	4·65	1·89
Ditto	18·1	7·41	4·65	2·76

LECTURE IV.¹

MR. PRESIDENT AND GENTLEMEN,—The third method which has been used in the study of the amount of heat produced under different conditions may be called the chemical. It need not detain us long, for the study of the chemistry of the heat-production of the body is so beset with difficulties that up to the present time not very much work has been done at this subject. There are two divisions of it—namely, the chemistry of the heat-production in the non-febrile and in the febrile states, and we will consider them in that order.

The breaking down of any chemically complex substance, such as a proteid or a fat, always leads to the liberation of energy. Various observers have, by burning these substances in a calorimeter, calculated the amount of heat set free by their destruction. In such a case the whole of the liberated energy appears as heat. Some of the most careful and recent results are Stohmann's.² His figures are gramme calories, and they represent the amount of heat necessary to raise one gramme of water from 17° to 18° C. They are shown in the following table.

TABLE XXVII.

—	Gramme calories.
The heat value of one gramme of most } albumins is } The heat value of one gramme of meat is... }	5298 to 5941
The heat value of one gramme of albuminoids is }	5662
The heat value of one gramme of chondrin } is }	4650 to 5961
The heat value of one gramme of animal } fat is }	5130
The heat value of one gramme of olive } oil is }	9509
The heat value of one gramme of carbohydrates is... .. }	9500
The heat value of one gramme of cane } sugar is }	4381 to 3714
	3955

¹ Delivered on June 29th.

² Ueber den Wärmewerth der Bestandtheile der Nahrungsmittel, Zeitschrift für Biologie, Band xxxi., Heft 3, S. 364.

These figures are, as we shall see in a moment, of great value; but I need hardly remind you that we cannot calculate the heat production of an animal from its diet. In the first place we do not know what proportion of any meal is absorbed from the gastro-intestinal tract; secondly, not all the energy set free in the body is manifested as heat; some takes the form of mechanical work, and therefore in calculating the heat value of any particular diet we should have to deduct the energy which in the body takes the form of motion, but this is very difficult to estimate accurately, and therefore the deduction to be made from the total heat value of the food would be uncertain; and, thirdly, the food may be stored up in the body and not broken down for some time. The value of figures, like those of Stohmann, which show the amount of heat produced by the breaking down of the albumins and fats of the body lies in the fact that we can, by observing the amount of nitrogen and carbon excreted, calculate what must have been the amount of proteid and fat which had to be broken down to produce these amounts of nitrogen and carbon, and then, by looking at Stohmann table, we find how many calories the breaking down of these proteids and fats gave rise to. But in these calculations we must remember that although the fats are completely broken down yet the proteids are not. Nearly all the proteid is, however, broken down to urea and uric acid; the excretion of these can be measured and the number of calories resulting from their complete destruction estimated; if this is done and the calories of energy remaining in the urea and uric acid are deducted from those set free if a gramme of albumin is broken down as low as possible, we, of course, easily obtain the energy value to the body of a gramme of albumin, and this is found to be about 4000 gramme calories.

Rubner³ has in animals, by careful analysis of the expired air, the urine, and the fæces, observed the amount of nitrogen and carbon excreted, from which he calculates the quantity of each of proteids and fats, which corresponds to such an amount of nitrogen and carbon. Then he compares the heat given off by the animal to an animal calorimeter with the heat that he would, from his knowledge of the number of calories set free by the breaking down of these quantities of proteids (after allowance for the urea and uric acid) and fats, expect to be produced by the animal during the time it was in the calorimeter. Table XXVIII. shows how the calories reckoned by each method correspond. It gives in kilogramme calories the results of experiments on a small dog which was observed for five days starving, five days on a fat diet, eight on a diet of meat and fat, and six on meat; and on a big dog observed two days starving, twelve days on meat and fat, and seven on meat. Each twenty-four

³ Die Quelle der Thierischen Wärme, Zeitschrift für Biologie, 1893-94 Band xxx.

hours was observed separately, and the table gives the total results for each dog for each diet. Rubner's experiments were very carefully performed, and therefore we must all look forward with great interest to their confirmation. If they are confirmed they will prove that he has successfully overcome many great difficulties, and the agreement between his chemical and calorimetical results will be remarkable, for, firstly, we have seen that animal calorimeters may be very inaccurate instruments and unless very carefully constructed will give rise to all sorts of errors. Secondly, the chemical method gives the heat produced, but the calorimeter only indicates that lost, and I have in the last lecture shown that we cannot infer quite accurately from that lost the amount produced by the animal, for we do not know whether during the experiment it varies its rate of loss, and, further, we cannot tell, unless we know the variations of its temperature during the twenty-four hours an experiment lasted, how much of its heat

TABLE XXVIII.

Diet.	Number of days.	Total of calculated heat.	Total of heat estimated by calorimeter.
Starving {	5	1296.3	1305.2
	2	1091.2	1056.6
Fat {	5	1510.1	1495.3
Meat and fat {	9	2492.4	2488.0
	12	3985.4	3958.4
Meat {	6	2249.8	2276.9
	7	4780.8	4769.3

production has been expended in raising its temperature, and if any has been so used it would not be shown by the calorimeter. In these experiments the dissipation of energy as mechanical motion does not interfere with the results, for the animals keep quiet in a cage which just fits them; and, further, such mechanical work would tell equally in both sets of figures, as also would the work done by the heart and respiratory muscles, most of which work becomes heat as it has to overcome friction.

We now pass on to a consideration of the experiments in which an attempt has been made to calculate the heat production of starving animals suffering from fever by observing the amount of nitrogen and carbon excreted. It is always necessary to use starving animals, for it is well known that the ingestion of a meal increases the production of heat, as, indeed, the table just quoted from Rubner shows. This method can give us some idea of the chemical processes

involved in fever, but in applying the results to man we must remember that as human patients are given food during a febrile illness, and as man has, by his sweating and hairless skin, far better means than the lower animals of varying his loss of heat, the processes may be somewhat different in man from the processes in a starving animal. By far the best experiments are those of May,⁴ and I am the more disposed to quote some of his results as I found, when Professor Burdon Sanderson's article on Fever in Professor Clifford Allbutt's System of Medicine appeared, that the high opinion I had formed of their value was confirmed. May begins by giving a history of the subject, and comes to the conclusion that the balance of evidence is that in febrile pyrexia the respiratory quotient is unaltered, that the excretion of CO₂ is not much increased, and that the brunt of the destruction falls on the proteids. He used rabbits in whom he induced swine erysipelas. For some days before the production of this fever they were starved so as to get their excretion of urea steady, and during the fever May most carefully observed the output of nitrogen and carbon both in the urine and the breath for more than twenty hours at a time, and he calculated what must have been the original amount of proteid and fat tissue which would, when broken down, correspond to the nitrogen and carbon he found excreted. Using Stohmann's heat values of proteid and fat, he was able to estimate the number of calories which would be set free by the destruction of these amounts of proteids and fat. The following experiment may be quoted (Table XXIX.). It shows distinctly that when a starving rabbit is suffering from swine erysipelas there is an increased heat production, and that this is due entirely to an increased destruction of proteid.

TABLE XXIX

Day.	Mean weight of rabbit.	Temperature of rabbit.	Calories.				Per kilogramme of animal.	Remarks.
			Nitrogen.	Sugar.	Fat.	Total.		
	Grms.	Deg. C.						
3	2832	38.5 38.2	47.56	—	105.1	152.66	53.8	—
4	2737	38.2 38.6	50.5	—	97.44	147.94	54.0	—
5	2632	38.6 38.6	54.25	—	91.55	145.80	55.4	—
6	2522	38.7 40.1	70.50	—	83.88	154.38	61.2	Fever
7	2384	40.1 38.1	64.75	—	99.87	164.62	69.1	Fever

⁴ Zeitschrift für Biologie, Band xxx., S. 1.

The following table of the results obtained by experiment upon three starving rabbits also shows very well how strikingly the destruction falls upon the proteids (Table XXX.).

TABLE XXX.

—	Day of observation.	Calories.		Remarks.
		From nitrogenous substances.	From non-nitrogenous substances.	
Rabbit E	3rd	18.0	44.0	{ Fever began. Fever.
	4th	19.0	45.0	
	5th	27.0	46.0	
Rabbit G	3rd	16.8	37.0	{ Fever began. Fever.
	4th	18.5	35.6	
	5th	20.6	34.8	
	6th	27.9	33.3	
Rabbit H	3rd	10.7	53.8	{ Fever began.
	4th	10.4	53.7	
	5th	11.8	54.0	

May's next experiments are of the greatest interest to clinical physicians. He gave a starving rabbit a known quantity of grape sugar and made—both before and after the administration of the grape sugar—observations similar to those I have just described. After the observations the animal was immediately killed, and the glycogen in the body and the grape sugar in the urine, alimentary canal, and fæces were estimated, and from the figures obtained May was able to learn how much had been used in the body. The following table shows very well how the administration of sugar saves the destruction of albumin and fat which goes on in starvation (Table XXXI.).

TABLE XXXI.

Day.	Mean weight of animal.	Calories.					Remarks.
		Nitrogen.	Sugar.	Fat.	Total.	Per kilo-gramme of animal.	
	Grammes						
4	2434	39.75	—	84.61	124.36	51.1	—
5	2394	30.00	92.93	—	122.93	51.3	{ Sugar given.

And the next table shows, too, how the administration of sugar effects a similar saving in fever (Table XXXII.).

TABLE XXXII

Day.	Temperature of animal.	Mean weight of animal.	Calories.				Per kilo-gramme of animal.	Remarks.
			Nitrogen.	Sugar.	Fat.	Total.		
	Deg. C.	Grms.						
4	{ 39.5 40.4	{ 2560	60.75	—	171.32	232.07	90.7	Fever
5	{ 39.6 39.8	{ 2462	32.25	94.56	45.17	171.98	70.0	Fever and sugar

Experimental medicine here shows strikingly why it is, as clinical medicine has found by experience, that milk and farinaceous diet is best for fever, and, further, as all May's experiments show conclusively that in starving rabbits suffering from swine erysipelas the heat production is increased, and that this increased production is due entirely to a greatly increased destruction of proteid, we are probably correct in concluding that in most fevers the greater part of any increased production of heat is due to an increased destruction of proteid rather than to an increased destruction of fats. It is true that May has not been able to allow for any energy which, resulting from the breaking down of tissue, manifested itself as mechanical work; but the increase of proteid destruction he found was so great that even if the fevered starving rabbit did a little more mechanical work than it did before the fever was induced the increased energy taking this form can have been only a small proportion of the whole energy resulting from the increased destruction of proteids. It is almost impossible to make any such observations on man, but some attempts have been made to find out whether in man the amount of CO₂ exhaled is increased during fever. Many more observations will have to be made on different fevers before the results can be accepted as final, but as far as they go they show that in man the amount of CO₂ excreted during fever is not increased. I will quote the results of two observers. Loewy⁵ gives the following table of observations made on a case of typhoid fever (Table XXXIII.). It is noteworthy that not only is there no increase in the output of CO₂, but also that the respiratory quotient is low for man, whose normal is 0.8 or rather over this, although, according to May, the balance of evidence is that in fever it is unaltered.

⁵ Virchow's Archiv, Band cxxvi., S. 218.

Kraus⁶ has also made a number of observations. He comes to the following conclusions: (1) That fever is possible when the oxidation processes (measured by determining the gaseous exchange) are not perceptibly increased, and this even during a long period in which the patient wastes; and (2) that the metabolic processes of fever do not markedly influence the respiratory quotient, which depends entirely on the condition of the patient. I ought to add

TABLE XXXIII.

CO ₂ output per minute in cubic centimetres.	O intake per minute cubic centimetres.	Respiratory quotient.	Body temperature.
			Deg. C.
183	280	0.653	38.3
221	265	0.853	39.3
190	279	0.682	39.5
205	291	0.706	39.8
198	320	0.620	39.7
248	323	0.706	39.2
277	325	0.851	} Normal three weeks after last observation.

that Zuntz, in a communication made to the Berlin Physiological Society, showed that different men under the same conditions varied very much in the amount of oxygen inhaled and the amount of CO₂ exhaled. Loewy and Kraus were, however, aware of this.

My work in this direction has been slight, for the only experiments I have done relate to the gaseous exchange of rabbits in which pyrexia had been induced by cerebral lesions and to that of hibernating dormice. Mr. Hopkins and I investigated the question of whether the output of CO₂ and and H₂O from the lungs was increased when pyrexia was induced by cerebral lesions. We used the differential calorimeter I have already described. The animal was shut in one chamber, no hydrogen was lit in the other chamber, but it was closed and an equal amount of air was drawn through each chamber. The outgoing air from each was passed through a pumice and sulphuric acid tube to absorb the water, then through a U tube containing pumice soaked in caustic potash, and then through two U tubes each containing dry caustic potash. The sulphuric acid tube was weighed before an experiment, and each set of three caustic potash tubes was also weighed, and the tubes were then again weighed after an experiment the duration of which was

⁶ Zeitschrift für Klinische Medizin, Band xviii., S. 160.

TABLE XXXIV.

Animal.	Date.	Hour.	Temperature of animal degrees F.	Grammes of CO ₂ given off by the animal per hour.	Grammes of CO ₂ in an amount of air equal to that breathed by the animal.	Grammes of H ₂ O given off by the animal per hour.	Grammes of H ₂ O in an amount of air equal to that breathed by the animal.	Remarks.
	1896							
	Feb. 25th	5 to 6 P.M.	100.8	2.945	0.85	1.19	0.61	—
	Feb. 26th	5 to 6 P.M.	100.8	3.26	1.01	1.34	1.21	—
	Feb. 27th	5 to 6 P.M.	99.8	2.64	0.21	1.25	1.30	6.30 P.M.: right corpus striatum punctured.
Rabbit A ...	Feb. 28th	10½ to 11¼ A.M.	102.4	2.98	0.22	0.97	2.05	—
	March 2nd	5 to 6 P.M.	100.1	2.88	0.58	1.03	0.67	—
	March 3rd	10½ to 11½ P.M.	101.3	2.97	0.38	1.32	1.31	1.45 P.M.: left corpus striatum punctured.
	March 4th	10½ to 11¼ A.M.	100.3	2.91	0.21	1.25	0.59	—
	March 23rd	5 to 6 P.M.	100.2	2.91	0.30	0.96	0.13	—
	March 24th	10½ to 11¼ P.M.	101.7	3.07	0.32	0.75	0.18	2 P.M.: right corpus striatum punctured.
Rabbit B ...	March 26th	10½ to 11½ A.M.	100.8	2.86	0.23	0.89	0.21	4.30 P.M.: left corpus striatum punctured.
	March 27th	1 to 2 A.M.	102.4	3.06	0.13	1.47	0.20	—

TABLE XXXV.

Dec. 22nd, 1895—Male Dormouse.				Dec. 22nd, 1895—Female Dormouse.			
Temperature of air.	Rectal temperature of mouse.	Time P.M.	Remarks.	Temperature of air.	Rectal temperature of mouse.	Time P.M.	Remarks.
Deg. C.	Deg. C.			Deg. C.	Deg. C.		
5.5	9.0	3.40	Quiet; coiled up.	5.5	9.0	3.40	Quiet; coiled up.
10.0	11.0	3.55	" "	10.0	10.5	3.55	" "
12.0	14.5	4.10	" "	12.0	14.25	4.10	" "
18.0	26.0	4.25	Awake.	18.0	18.5	4.25	Awake.
17.0	28.0	4.40	"	17.0	23.0	4.40	"
20.0	33.0	4.55	"	20.0	30.0	4.55	"
20.5	33.0	5.10	"	20.5	32.5	5.10	"
18.5	33.25	5.25	"	18.5	32.25	5.25	"
7.0	30.0	5.45	Very lively	7.0	36.0	5.45	Very lively.
7.0	31.0	6.0	"	7.0	34.0	6.0	"
7.0	31.0	6.30	"	7.0	33.0	6.30	"
6.5	29.0	7.0	"	6.5	33.0	7.0	"
6.5	30.5	7.30	"	6.5	31.0	7.30	"
6.0	34.0	8.30	"	6.0	34.0	8.30	"

usually an hour. Of course, the sulphuric acid tube and caustic potash tubes on the animal side gained more than those on the other side, for these only showed the H_2O and CO_2 in the air drawn through, while those on the animal side showed this, and in addition the H_2O and CO_2 exhaled by the animal in one hour and taken up in the air current passing through the chamber. By subtraction we found how much H_2O and CO_2 were produced by the animal. The annexed table (Table XXXIV.) shows the results of four experiments on two rabbits.

It will be seen that the excretion of CO_2 was not in Rabbit A strikingly increased by the pyrexia due to the cerebral lesion, for although after both operations it was a little higher than immediately before, yet after neither was it so high as on two days before any operation. In Rabbit B there does appear to be a slight increase after each operation, but I think you will agree with me that the variations in both animals are so slight and so well within the normal variations that we may conclude that damage to the corpus striatum does not increase the output of CO_2 , and in this respect the pyrexia which follows it is similar to the pyrexia which accompanies those fevers in which the excretion of CO_2 has been investigated. Inspection of the figures also shows that the pyrexia caused no constant alteration in the amount of aqueous vapour exhaled. It will be noticed also that it is impossible to trace any relationship between the CO_2 and H_2O in the air and that exhaled by the animal. I need hardly add that the position of the lesion in the brain was always confirmed by a post-mortem examination.

Dr. Pembrey and I have performed a number of experiments upon hibernating dormice.⁷ When these creatures are hibernating their temperature is very low, the rectal temperature usually being about 9° or $10^\circ C.$; if they are brought out of a cold into a warm atmosphere their temperature slowly mounts at about the same rate as that of an equal weight of water (for their specific heat is very little less than that of water) until it reaches about $16^\circ C.$, when it suddenly mounts many degrees in a few minutes to between 33° and $36^\circ C.$; at the same time the sleepy animal becomes active and runs about. The accompanying table shows this rise (Table XXXV.), and it also shows that mere lowness of external temperature will not cause the animal to sleep or its temperature to fall. This will only happen when lowness of external temperature causes the creature to become inactive. This fact is very well shown in Table XXXVI.

Our observations brought out the interesting fact that this characteristic sudden rise of the animal's temperature was always associated with an equally sudden increase in the output of carbonic acid. The animal was placed in a chamber through which air was drawn, and the temperature of the air in the chamber was varied by alterations in the temperature of a water bath. As the air left the chamber the

⁷ Journal of Physiology, vol. xix., Nos. 5 and 6.

TABLE XXXVI.—*Dec. 29th, 1895 : Female Dormouse.*

Temperature of air.	Rectal temperature of mouse.	Time P.M.	Remarks.
Deg. C.	Deg. C.		
21.25	33.5	12.15	Wide awake and running about.
9.5	34.5	12.30	" "
9.5	29.0	1.0	" "
9.25	30.5	1.45	" "
9.25	18.0	2.30	Coiled up, begun to sleep, eyes still open.
9.25	14.5	3.0	Coiled up, fast asleep, eyes shut.
9.25	14.5	3.30	" "
10.0	14.5	4.30	" "
9.25	11.0	7.0	Coiled up, very fast asleep.

CO₂ in it was determined, a separate determination being made for each variation in the temperature of the air in the chamber. The following table (Table XXXVII.) shows very well this great increase in the output of CO₂; and the next table shows that, like the temperature, the output of CO₂ depends, not upon the external temperature, but upon the activity of the animal (see Table XXXVIII.).

TABLE XXXVII.—*Lormouse No. 1, Sept. 21st, 1894.—The active dormouse was in the ventilated chamber—water-bath = 25° C.—for thirty-five minutes before the first period. Temperature of the air of the room = 13° C. Consecutive periods of fifteen minutes.*

Temperature of water-bath.	CO ₂ discharged in decigrammes.	Remarks on the dormouse.
Deg. C.		
25.0	236	Active; washing itself.
23.75	173	Quiet.
25.5	188	Quiet, coiled up, apparently asleep.
15.0	183	Woke up for a moment, then quickly coiled itself up.
15.0	59	Quiet, coiled up.
24.25	23	" "
25.0	20	" "
24.5	159	Awakes towards the end of this period.
25.0	335	Awake, but fairly quiet.

TABLE XXXVIII—*Dormouse No. 1,* Sept. 24th, 1894.*—
The sleepy dormouse was in the ventilated chamber—
water-bath = 25° C.—for thirty minutes before the first
period. Temperature of the air of room = 15° C.; con-
secutive periods of fifteen minutes.

Temperature of water-bath.	CO ₂ discharged in decigrammes.	Remarks on the dormouse.
Deg. C.		
25·0	113	Coiled up.
24·75	112	"
15·0	220	Active at first; then coiled up.
15·0	68	Coiled up.
15·0	21	"
25·0	17	"
25·0	14	"
25·0	20	"
24·5	25	"
24·75	20	"

* The dormouse was coiled up and fast asleep at the end of the experiment.

We learn, therefore, that the rise of temperature which occurs when hibernating dormice become active is unlike the rise of temperature which occurs when a rabbit is afflicted with swine erysipelas or has its temperature raised by damage to the corpus striatum, for it is accompanied by an enormous increase in the output of carbonic acid. This goes to show what is probably true—namely, that the metabolic processes of the pyrexia due to cerebral lesions and of that due to fever are quite different from those of health, and not merely an exaggeration of these.

I think now we have come to the end of our discussion of the problem of the variations in the production and loss of heat in pyrexia, and the three great main conclusions to which we seem to have come are:—1. In man at least pyrexia is not produced by the same method in all fevers; sometimes the rise of temperature is due to an increased production of heat, and sometimes to a diminution of the loss. 2. In the present state of our knowledge animal calorimetry is very difficult, and the results obtained from calorimeters must be received very guardedly, especially when they are applied to man. 3. In some forms of pyrexia in which the production of heat is increased the metabolism leading to this takes place in the proteid tissues of the body, and probably the metabolic processes concerned in a pathological rise of temperature are different from those of health.

A very difficult problem which has been much occupying the minds of the profession lately has been that of why

almost all micro-organisms which are harmful to the body raise its temperature, and the suggestion has been made that the rise of temperature is a defensive mechanism, or, in other words, pyrexia is, like phagocytosis or chemiotaxis, in some way harmful to the fever-producing micro-organisms or their toxins. Of course, it does not follow from this view that the higher the temperature of the body the better the prognosis, for the higher temperature might be taken to indicate that the dose of infection was very severe, and that therefore the body did all it could to resist the invasion, nor, on the other hand, would it follow that if the temperature did not rise much the dose of infection was slight, for it might be that the body was feeble and had but little power of raising its temperature and therefore defending itself. We see, therefore, that clinical observation can hardly settle the point, but in passing I may mention that I have seen a severe case of typhoid fever in which during the second week of the illness the temperature was very irregular; the patient, however, always felt better and had a better pulse when her temperature was high than when it was low.

A few years ago much was hoped from the antipyretic drugs—antipyrin, acetanilide, and phenacetin; and if it could have been shown that they distinctly improved the condition of the fevered patient it would have been a strong argument against the view that pyrexia is a defensive mechanism. The reverse, however, is the case, for they are not now often employed as antipyretics, and in a discussion on pyrexia and its treatment which took place at the Bristol meeting of the British Medical Association held in 1894, speaker after speaker got up and said that, as a general rule, it did more harm than good to treat the pyrexia of fever.

Some few fevers are treated by agents which lower the temperature, but these very fevers are instances of the exception proving the rule. Ague is treated by quinine, the temperature falls and the patient is better. This, however, is not because the quinine is an antipyretic, but because it is a poison to the plasmodium malarie; the patient's temperature falls because the pyrexial agent is destroyed. The same is true of syphilis. If a patient is suffering from syphilitic fever his temperature falls when he takes mercury, not because mercury is an antipyretic, but because the cause of the pyrexia is destroyed. Again, it is almost certain that any benefit that follows in rheumatic fever from the administration of salicylates is not due to their antipyretic action, but because they are specifics for rheumatic fever, for other antipyretics are not equally efficacious, and salicylates benefit other symptoms than the temperature—viz., the pain. It is generally believed, and in all probability correctly, that most cases of typhoid fever are benefited by cold sponging or by a cool bath. Many have hastily concluded that the bath does good because it lowers the temperature. But this is probably incorrect. In the first place we must remember that the cold sponging or bath does more than lower the temperature; it diminishes the delirium, the tremor, and the prostration. In

any of these ways it would do good. But, further, Roque and Weil claim to have shown that "in typhoid fever left to itself the toxic products manufactured by the bacillus and organism are eliminated in part during the illness. The urotoxic coefficient is double the normal, but this elimination is incomplete and is only completed during convalescence, for the hypertoxicity continues for four or five weeks after the cessation of the fever. In typhoid fever treated by cold baths the elimination of toxic products is enormous during the illness. The urotoxic coefficient is five or six times the normal. The hypertoxicity diminishes as the general symptoms mend and as the temperature falls, so that when the period of pyrexia and convalescence sets in the elimination of toxins has ceased." So we learn that it is by no means certain that in typhoid fever the benefit of cold baths is due to their antipyretic influence, and we see that clinical medicine affords no evidence that antipyretics are useful in fever.

I had hoped to be able to lay before you some original observations bearing on the question of whether or not pyrexia is a protective mechanism, but, unfortunately, I have not had time to carry them out, and therefore I must content myself with giving you briefly those of others. The best collection of the literature of this subject is given by Max Muller,⁸ and many of the following references are quoted from him. Heydenreich⁹ found that the spirillum of relapsing fever lost its mobility quicker at 40° C. than at 37° C., while at from 15° to 22° C. it retained it a long time. Then in 1880 Pasteur¹⁰ made the observation that fowls which were ordinarily refractive against anthrax bacilli succumbed to them if their temperature had been artificially lowered by their being cooled, and in the same publication next year he said he had found that the virulence of anthrax bacilli is diminished by a temperature of from 42° to 45° C. Wagner¹¹ infected fowls with anthrax bacilli and spores, and kept down the temperature of some of them by partially immersing their bodies in water; these succumbed, but others left at the ordinary temperature did not. He also infected a series of eleven in whom the temperature was kept down by antipyrin; of these eleven six were taken ill; and of these six five died. This, he thought, was due to a lowering of the temperature by antipyrin. Rovighi, in a paper abstracted in volume vii. of the same *Centralblatt*, gives an account of how he infected three series of rabbits with saliva; one lot were placed in an incubator the temperature of which varied from 37° to 42°, another lot were left at the ordinary temperature, and the third lot were artificially cooled. He found the mortality to

⁸ Wirkung der Fiebertemperatur auf den Typhusbacillus, Zeitschrift für Hygiene und Infectiouskrankheiten, 1895, S. 244.

⁹ Centralblatt für die Medicinischen Wissenschaften, 1876, No. 28.

¹⁰ Charbon et Septicémie, Comptes Rendus, 1880.

¹¹ Centralblatt für Bakteriologie und Parasitenkunde, 1881, Band ix.

be highest among those artificially cooled and least among those artificially warmed; and in the same periodical for the year 1891 it will be found to be stated that Walther observed that after infecting rabbits with the pneumococcus those placed in a warm oven lived longer than those placed at the ordinary temperature of the room. Koch found that if tubercle bacilli were kept at a temperature of 42° C. for three weeks their development was much hindered, while the best temperature for their development was from 37° to 38° C. We thus see that this bacillus, the scourge of the human race, flourishes best at the internal temperature of man, and it is quite possible that if a phthisical patient's temperature could be safely kept at 108° F. for a month he might be cured. Fränkel¹² finds that the pneumococcus named after him loses its influence on rabbits in twenty-four hours if they are kept at a temperature of 42° C. Both Bumm and Finger have observed that the temperature at which the gonococcus flourishes best is between 33° and 37° C., and that higher temperatures stop its development. Max Muller came to the conclusion that the higher the temperature the less rapidly typhus bacilli multiplied. Welender and Berlien¹³ have been treating soft sores by means of a thermostat, an instrument which keeps the sore at a temperature of 41° C., and they claim excellent results for this treatment. Filehne, at a meeting of the Physiological Society held at Oxford on August 11th, 1894, gave an account of some experiments in which he infected rabbits with erysipelas and studied the changes at the seat of infection, the ear. In animals kept in a warm chamber the reaction in the ear was slight, and attained its height in two days and the animal was soon well. In animals kept at the ordinary temperature the reaction was much more severe, and lasted ten or eleven days. In animals kept in a cool chamber nothing happened so long as they remained there, but as soon as they were taken out and left at the temperature of the room they had a very severe attack of erysipelas.

Loewy and Richter¹⁴ caused a rise of temperature in rabbits by puncture of their corpora striata; they then infected them with the bacilli of diphtheria, fowl cholera, swine erysipelas, and pneumonia. They came to the following conclusions: (1) that with very large fatal doses the animals whose corpus striatum was punctured lived longer than the control animals; (2) if the animals whose corpus striatum was punctured had a dose two or three times as large as that necessary to kill an ordinary animal they recovered; and (3) when a local injection of swine erysipelas was made into a rabbit's ear the local reaction was most marked in those animals in whom the corpus striatum had been punctured, but they invariably got quite well.

¹² Grundriss der Bakterienkunde, 1887.

¹³ Norddeutsches Medicinisches Archiv, 1895, No. 12.

¹⁴ Ueber den Einfluss von Fieber und Leucocytose auf den Verlauf von Infektionskrankheiten, Berliner Klinische Wochenschrift, 1895, No. 15.

I quite admit that all these observations do not prove that pyrexia is a protective mechanism, but they certainly suggest that it is, and many who have thought about the subject have given their adhesion to this view; such, for instance, are Roy,¹⁵ Cantani,¹⁶ and Sanarelli.¹⁷

It struck me some time ago that if pyrexia is a protective mechanism it might be a good thing to administer to fevered patients drugs that would raise their temperature, if before doing this it could be shown by laboratory experiments that such drugs have the power of diminishing the severity of fevers. There are many pyretic drugs. The temperature may rise to 104° F. as a result of belladonna poisoning. In animals, at least, large doses of cocaine will cause a rise of temperature. It is said the best dose for producing this effect is a subcutaneous injection about eight milligrammes per kilogramme of the animal, the dose to be frequently repeated. Strychnine and caffeine, too, will both raise the temperature a little. But by far the most important drug for raising the bodily temperature is β -tetrahydronaphthylamine. Some remarkable experiments concerning this drug are given by Stern.¹⁸ For instance, he took a rabbit weighing 1600 grammes, the temperature of which was 40° C., and at 10.42 A.M. injected subcutaneously 0.075 grammes of β -tetrahydronaphthylamine. The temperature was taken every few minutes afterwards with the following results:— At 10.55 A.M. the temperature was 40° C.; at 11.0 A.M. it was 40.2°; at 11.8 A.M. it was 40.9°; at 11.20 A.M. it was 41.4°; at 11.40 A.M. it was 43.0°; at 11.52 A.M. it was 44.5°; and at 12.2 P.M. the rabbit died. So that the drug actually raised the temperature 4.5° C. in an hour. By giving a smaller dose of the drug he was able to obtain a considerable rise of temperature without killing the animal.

Such a remarkable drug appeared to me to be worthy of further investigation, and Dr. J. Fawcett agreeing with me we made some experiments. We employed a 3 per cent. aqueous solution and always gave it subcutaneously. We performed several experiments; the following are the details of one.

The rabbit weighed 2400 grammes. At 1.30 P.M. the rectal temperature before injection was 38.7° C.; at 1.35 P.M. 3 c.c. of the solution were injected; at 1.55 P.M. the temperature had risen to 39.3°; at 2.10 P.M. it was 40.5°; at 3.5 P.M. it was 41.5°; at 4 P.M. it reached 41.9°; and from 4.30 to 7 P.M. it gradually fell to 39.3°. The following table (Table XXXIX.) shows the results of all our experiments.

It will be seen that in one animal a rise of 5.5° C. took place. This died, but all the others recovered, and in one of them there was a rise of as much as 3.2° C. In all

¹⁵ Brit. Med. Jour., vol. ii., 1893.

¹⁶ Transactions of the International Medical Congress at Berlin, 1890.

¹⁷ Annales d'Institut Pasteur, April, 1894.

¹⁸ Virchow's Archiv, 1889, S. 14.

TABLE XXXIX.—*Showing the result of injecting a 3 per cent. solution of β -tetrahydronaphthylamine subcutaneously in five rabbits.*

Number of experiment.	Weight of rabbit in grammes.	Dose injected.	Time taken to attain maximum temperature.	Temperature at beginning in degrees F.	Temperature at end in degrees F.	Rise in degrees F.	Rise in degrees C.	Remarks.
1.	2400	3 c.c.	3 hrs.	101.6	107.4	5.8	3.2	—
2.	2050	3 c.c.	1 $\frac{3}{4}$ hrs.	102.7	112.6	9.9	5.5	This animal died; greatest rise.
3.	3570	4 c.c.	2 hrs.	103.1	106.8	3.7	2.1	
4.	2200	3 c.c.	2 $\frac{1}{2}$ hrs.	101.4	104.3	2.9	1.6	Least rise.
5.	2200	3.5 c.c.	4 hrs.	101.8	105.0	3.2	2.2	

five experiments the pulse and respiration were enormously increased in rapidity, often both were so quick that they were quite uncountable. We never observed any of the variations in the size of the pupil or the vessels of the eye that Stern mentions. As animals which, like rabbits, do not perspire much must lose most of the heat they part with by the lungs, the rise of temperature produced by β -tetrahydronaphthylamine cannot have been due to a diminution of the loss of heat. Indeed, judging by the rapidity of respiration, this must have been much more rapid than usual, and probably the creature was by increasing its heat loss struggling against the rise of temperature produced by the drug. The animals for an hour or two after the drug was injected were usually rather restless, frequently shifting their position and turning round, but they never ran about or made any prolonged severe muscular movement. This restlessness was always followed by marked loss of muscular power, but nevertheless the temperature continued to rise. The only animal that had convulsions was the one that died, and they did not appear until shortly before death. These facts seem to me to be strongly in favour of the view that the drug has in some way greatly increased the production of heat, and that this increased production is not due to muscular movement, for the rise is altogether too great and too rapid for it to be caused even in large part by the increased muscular movement due to the greater rapidity of the respiration and pulse. In support of this view I may mention that Stern was also of opinion that the muscular movements were not

sufficient to explain the rise of temperature, for in his experiments this sometimes occurred in animals which were quiet without any drug being given to keep them quiet, and also in those which were kept quiet by morphia. Further, the rise of temperature that is seen in animals convulsed with strychnine is never nearly so great as that produced by β -tetrahydronaphthylamine, although rabbits under the influence of this drug never show muscular contractions comparable to those produced by strychnine. Then, too, some experiments performed by Mosso go to show that even the comparatively slight rise of temperature in strychnine poisoning is not due solely to muscular contractions. I cannot help thinking, therefore, that we have in β -tetrahydronaphthylamine a drug which stimulates the thermogenetic without exciting the motor function of muscle, and that therefore we see—as we have already seen in the patients afflicted with hemiplegia—that the two functions are distinct.

I have already pointed out in these lectures that damage to the corpus striatum produces a considerable rise of temperature. The rise produced by β -tetrahydronaphthylamine so resembles in extent and rapidity that caused by these injuries that it is at least likely that the drug acts on the muscles through the central nervous system. Dr. Fawcett and I tried to find out whether this was so, but all the experiments we could devise necessitated fixing the animal down and performing artificial respiration, and, as I have already pointed out, this interferes so much with the animal's temperature that we were unable to obtain any satisfactory answer to the question we attempted to solve.

I have not yet had time to see whether the administration of this drug increases the resistance to any febrile diseases, but it is clear that even if it does it will have to be given very cautiously to man on account of its marked effect on the heart.

The only duty that now remains to me is to thank you for having listened to these lectures, and to express my regret that they should have been so imperfect and fragmentary. This is, for the most part, my fault, but it is also due to the difficulties of the subject. I have not referred to the work of many to whom reference should be made were I writing a full account of pyrexia; this is because I believed the founder's wish to be that lecturers should relate what they themselves had done and thought rather than that they should give a condensed account of what others had done and thought.





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