An Essay on

Our Present Knowledge of the Condition of Fungi

Being the Thesis submitted to the Faculty of Medicine, University of Edinburgh, for the Degree of Doctor of Medicine.

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On the Process of Fever.

The afternoon about 5 o'clock, I saw a little girl, 8 years old. She had been playing about all day and seemed to be in perfect health. She came in, complaining of feeling ill by headache, went to bed speedily, became unconscious, then I reached the house an hour or two after she had been taken poorly. She was lying about in bed, restless, delirious. The temperature in the arilla was 105.9. The pulse very rapid, the respirations somewhat quickened, though not so much as the pulse in proportion. The digestion had appeared to be normal. The chest quite healthy, the breath all cut, except for the delirium. The vision is to be expected with the usual signs of disturbance in the nervous system. The day was hot, a hot one, there had been little or no sunshine.

Next morning the child was running about again, apparently quite well. The temperature the pulse both being normal. There was no return of the trouble.
On Saturday, Sept 19th 1891 a man of 56 had a rigor with pains in the back headache followed by a copious discharge of urine loaded with albumen. In the following afternoon he had another rigor which was attended by the same symptoms. Immediately after he was found to have a temperature of 103°, the pulse 36, the respiration 18. Except headache, there was nothing complained of except the above. The lungs were kept up for today, getting gradually lower each day. During the whole time, nothing more could be discovered except a metapneumonia keeping very little above the normal.

As to the cause of the disturbance, nothing could be traced except that for two or three weeks he had had a great deal of worry and anxiety.

Such are the fairly typical cases of what one constantly sees in practice—cases of meningitis (usually with the concomitant dry skin, thirst, tarry tongue, quickened pulse, respiration etc.) being the only thing present for diagnosis treatment.
Without going into further detail about these cases, I wish to use them as an introduction to a discussion on the subject.

Pyrexia or Fever

The phenomena of fever are constantly presented to the medical man. In the great majority of cases of illness, fever is present; it is probably the commonest of all the factors of disease. Almost any disturbing influence is capable of setting up the condition. It accompanies the most varied forms of disease.

Not only is it a constant symptom of the group of fever (specifically so-called), it is also to be found in inflammation of almost all areas of the body. It follows the infliction of mechanical injuries to all parts—the excluding the nervous system itself—which it may be produced artificially by the injection into the blood of different substances—such as for the case—albuminoses, acrid acids. Its frequency suggests that it has a very close
connection with the origin of disease, that its relationship is fundamental. And one can hardly be driven to think that if one could thoroughly understand the proximate, immediate causation of the process of fever, one could do a great deal towards elucidating the causes and conditions of disease of all kinds.

It is important to recognize from the earliest times until quite recently, that a considerable proportion of their space was devoted to its consideration. In old times that, for long ages, as Salmon says, the theory of the treatment of it became the theory of the treatment of all the rest. More attention has been paid to it than to any other subject in medicine, but until the last few years, it was little more than the plaything of the wise. And although it still lends itself to much theorizing, yet more attention has been paid to the things that really happen in the process, therefore, better grounds for theory have been given that substantial progress in the understanding of it made.
As for a definition of fever perhaps it is best today that fever is one of those things that cannot be defined, but as a working definition is almost necessary, there seems little doubt that that of P. F. W. being as it is so general, flexible and as it does not hold that is controversial strictly theoretical, is the most useful.

"Neque essentia quidem febris est in calore, sed in aliis." Perhaps a still better is the modification of it by Dr. Macalister, who said "fever is that disordered condition of the body heat, whose frequent symptoms manifest serious sign is high temperature. The temperature is not necessarily high. For the temperature is not necessarily high. In exceptional cases it is actually sub-normal (Plus sine febre).

All the other definitions, like heat of secretion (that form consists essentially in elevation of temperature which usually arises from an increased tissue change, over to have its immediate cause in alteration of the deviour of the system) being in an element of the body in which is better defined from a definition of Macalister. The halt of Forth p. 1887 (Macalister).
Symptoms.
The most constant symptom is increase in the body heat. But there are generally others such as increase of the cardiac respiratory rhythm, disturbance of the function of the renurc system (for example, albumen, coma, convulsions, excitation). Also disorder of the secretions of the intestine of the body causing dry tongue - thirst - constipation.

But the fundamental one seems to be that in which the cause exists - disordered body heat - fits in this which has to be chiefly kept in mind in thinking of the condition of fever. That this is so may be inferred from the following among other reasons.

1. It is the most constant symptom.

It is possible that a temperature be found without one or more of the other symptoms, but there cannot be fever without disorder of the body heat. As a rule the disorder is of such a kind that the temperature is above normal, but, as has just been said, there are exceptional cases in which the temperature is below normal. In these cases, however, there is elevation of temperature during a long or short period of time.
It is the only one that could cause the others.

Thus one often finds certain of the nervous symptoms that accompany fever (delirium, convulsions, restlessness, coma). The rise of temperature, increased frequency of pulse and breathing, this odd's reaction. Anaphylaxis of this are seen in epilepsy, the certain cases of cerebral hemorrhage.

Again, acceleration of pulse, respiration, and still more certainly the accompanying momentary disease. Many diseases furnish examples.

Abnormal nutrition indicates may also exist without any of the other symptoms. For example, overfeeding, indigestion, in cases of those of the stomach, defective secretion of the liver to the glands. Each of these forms of disturbed nutrition may exist alone.

(3) The application of heat is capable of causing the increased temperature also the other symptoms of fever.

(2) The application of heat in the Turkish bath may cause elevation of temperature.

[Signature]

W. J. T. Wilkie, Warden, H.M. Prison, Leeds, N.Z.
before the Leeds West Riding Medical
Chirurgical Society; and then before
the British Medical Association
(Physiological Section) when it met in
Manchester—giving details of a series
of observations on the temperature of
persons in the Danish Rumpballe.
Refound that out of 34 cases, the
temperature rose in 20—from 29
degrees centigrade to as high as 104.7
and 104.9 degrees.
(b) The condition of sunstroke (1) in which the
chief symptoms are high temperature,
headache, delirium, restlessness, coma,
with a diminished secretion, increased
rapidity of the circulation, & respiration
is caused by the external application
of heat of the sun.

The experiments have been performed by Dr.
Cameren Blum so on frogs, rabbits, & by Dr. Wood
on dogs & cats by others, which go to
confirm the statement that the external
application of heat may produce the same
symptoms. Heat was applied to the head
or to the head & conditions resulted of
quite comparable to those seen in sunstroke.

(1) Burdick, Observ. on the effects of
heat on the body, Phil. Trans. 1795.
(2) Fain, A Study in Medical Thermale Physiology, in
H. C. Wood, pp. 69-76.
- in the one case symptoms of brain damage,
- since being specially indicated for the
other disturbances of the circulation.
Application of heat to the whole of the body
also caused all the symptoms of fever.
Such experiments, though useful as far as
they go, are, however, conclusive and
are good only as confirmatory evidence.
The conditions of heat production in heat
in the cold blooded frog and the test coated
frog heart in which all of the heat has
be dissipated from the lungs are so different
from those in man that it is impossible
to judge from one to the other.
These considerations are, however, sufficient
to show that the order of the body heat is a truly
that the essential question is from the one
that might be studied.
But it is not such as to touch the actual
interrelation of the body heat has the heat within
the factors which govern that interrelation. That
interrelation is depends largely on the
relationship at the time between the heat
produced by the heat for.
In health there is at least a mechanism
which governs heat production. These conditions are kept so finely balanced that the temperature remains practically constant. The application of heat or cold, the giving or the withdrawal of food, the presence or absence of exercise, circumstances which do not influence bodily production nor all these things are not allowed to alter the temperature of the body. The variations which take place in relation to the time of day, heat, frost, are very slight indeed. In short, this mechanism would appear to be deranged, or else there seems to be a constant tendency to keep within prescribed bounds, yet the balance is not perfectly kept as in health. The temperature, therefore, is not the same; it is not constant.

**Heat Dissipation.**

The loss of heat from the body is mainly by perspiration, which escapes through the skin by evaporation, and by conduction and radiation. 77.5% is said to be lost in this way. The amount depends on the vascularity of the skin. The more delicate the arteries, the more heat being lost. This is controlled by the vasomotor centres in the medulla of the cord.

*Botto's Physiology*, p. 420, 3rd Edn. 1879.
30-99% more is lost by the lungs. the amount being greater, the more ample frequent the respirations. this is under the influence of the respiratory center in the medulla.

A much smaller quantity of heat - 0.6% is lost through the various excretions (kidneys, stool) but it is so small as to be almost disregarded.

heat production.

The question of the production of heat is not so simple as that of the loss.

Various kinds of energy, such as mechanical, chemical, electrical, are produced in the body. All forms of energy tend to assume the form of the least specialized heat. There is no doubt that all the others are directly or indirectly being transformed into heat.

The great sources of heat in the body are the food taken by the stomach, the oxygen utilized by the lungs. The food is altered in the stomach so that it is carried by the tissues where it is stored in complex combinations till it is needed.

The oxygen is carried to these other tissues by the blood. Fresh combinations result. thermal energy is manifested.

(1) Ford’s Physiology, p. 428. 1430
Although all the forms of energy go to increase the sum of heat produced, far the most important source of it is the chemical energy stored in the tissues. From this it is generally considered that the heat produced in the body is obtained.

Of all the tissues, the muscles are by a long way the greatest source of heat. They constitute half the bulk of the body, including the bones which are comparatively light. The nature of the chemical changes which take place in them is such as to contribute to the production of heat. If the muscles be thrown out of action by poisoning or amputation of heat produced by the animal is very small.

"The share of the muscles in the vegetative metabolism in the combustion processes of the body is so great that when they are excluded a mere fraction of the heat alone remains." (2)

Other tissues also contribute, especially the secreting glands which, without doubt, some heat is produced in the alimentary canal by the chemical changes in the food. (3)

Whenever a muscle contracts, heat is

(1) Foster: Physiology, p. 426.
(2) Alcalde: The Spirit of Man, p. 159, 127.
(3) Foster: Physiology, p. 428.
produced it has been supposed that the function of producing heat is intimately associated with that of producing work—that one is a measure of the other. That one bears a definite relation to the other. At the last International Medical Congress in Berlin, when this subject was discussed, there was a great difference of opinion on this point. Some, as Chaumeau, contended that this was the case for them, as Von Frey showed, denied it.

But there can be no doubt that the two functions are quite separate; this [is] that one does not depend directly on the other. Thus (1) during sleep there is very little muscular movement and the temperature of the body is fully maintained. (b) In many cases of cerebral haemorrhage the muscles are paralyzed, yet not only is the temperature at or above normal but the production of heat is actually increased. (2) Dr. Macal･[...]-in-experiments with the leg of a frog, with dogs, rabbits, guinea-pigs, found that the extensive stimulation brought about the production of the heat-producing function.

before the world producing (2) that coal
abolished the thermogenesis, while the con-
struction remained little or not at all impaired
(3) that the relation between work heat varied
between within limits.

That the chemical changes are those
are concerned in the production of heat these
two kinds of energy—thermal mechanical,
is quali in question. It is not even known
whether the same changes suffice for both
or whether there are two distinct mechanisms.
But the characteristic changes are the in-
negative in kind—the splitting up of complex
substances or the oxidation of them.

"The origin of heat in the body is best to be
attributed solely to the combination of
oxygen with organic material but that
in the separation of bodies which become
only in part oxidised is to be found
a rich source of animal heat."(1)
Infirmary. The essential objection is disorders of body heat—the sign of which is rise in temperature. Now as the elements which enter into this are loss of production of heat, it is evident that either more heat is produced or less lost than in health. And in recent years a great deal of the research has been directed to this point, 'Which of these is it?' And according to the results obtained leave different theories been built.

And now before we are in so satisfactory good a position to build a satisfactory theory, for especially during the last 20 years much has been added to our knowledge of the processes. We are now in possession of so many reliable trustworthy experiments, observations that the way seems comparatively clear.

But, before passing to the question of whether or not there is an increase in production or diminished loss of heat, it may be worth while to glance for a moment at the theory of Dr. suggested by Pasteur.

The theory is thus expressed by Dr. Pasteur (vol. 1. p. 40).

Ageneia consists not in a mere rise of temperature or increase in heat-generation.
"with diminished loss, but in a change in the "normal function of heat-regulation by "which production rates are so balanced "to enable maintenance of a temperature "higher than normal."

And when we treat the kind of chart seen in cases, say, of typhus fever, there to see that there is some battle in the body. But the similarity of the temperature curve in these cases to that of health indicates only that the same laws, the same mechanisms are at work in both instances, all leading to keep the temper-

ature within certain bounds.

And when we remember how very unstable the temperature is in fever, always liable to jump up and down, when we remember that in the majority of cases in which fever is present, this resemblance is not to be found, we are bound to confess that the theory rests on an insufficient basis of fact."
The Dissipation of Heat.

A theory of fever which fora long time was that of Scarpa (supported at the present time by Rovelli et al.). Scarpa supposed that the heat of the body was controlled by the organs which control heat dissipation. That when the temperature tended to be too high, more heat was lost; when too low, channels were shut, heat was kept in. In fever, the skin feels dry. Any condition is often related in life to rigor. And this leads one to suppose that there was abnormal retention of heat, the temperature rising because less heat was lost. This theory held it for granted that less heat was lost. If it could be shown that the contrary was the case, the theory would fall to the ground.

And many considerations present themselves which enable it appears probable that on the contrary, more heat passes from the body rather than less. Thus, it is quite obvious that to far from there being a constant passage of the arterioles of the skin, the surface is often flushed of the vessels diluted that the state of the vessels is

\[ \text{(R. Klein, loc. cit., Aug. 16, 91. Extract from Supplement R. Klein., 1881, 339.)} \]
Constantly changing, sometimes dilated and sometimes contracted. And besides, the length of the skin is always changing in shape or position, and the temperature of the skin is always changing in respect to its relation to the surrounding air, showing that the amount lost is always varying.

There has now been accumulated a mass of evidence which from direct experiment—which the writer believes the question that has been through all ages—had been treated by the ancients.

(a) Those on man and (b) those made on lower animals.

(b) Experiments with man.

These are among the most valuable that have been carried out by Liebermeister in Switzerland. Liebermeister placed fevered patients in cold water to measure their heat, and compared the results with those of healthy patients. He found that in every case the fevered patient raised the temperature of the bath more than the cold. Thereby the loss of heat from the fevered was greater than from the cold.

Objections have been made to these experiments:

(1) That evaporation by which heat is lost, can take place both in the cold bath (calculated).

But this would apply equally both for the well. What fever I could at the well, be an absolute quantity of heat lost first to the relative.

(2) That, as the production of heat is stimulated by the application of cold, the effect of the bath to produce increase of heat would be less in the former than in the latter.

The apparent difference in the temperature of the bath is the difference of the heat, being so different.

But, even if this be allowed, the difference would again be at the two, only quantitatively. The conditions would literally a little exaggeration of the actual ones when the bodies are in air stilled in water. Just as the bath would be relatively colder to the praise than to the well, so is the air of the room in which they would other-wise be.

(3) Experiments confirm the view of Weber, Mende, and made by a different man. He put the head of a person in a
Calorimeter measured the amount of heat given off. He then noticed the difference between the powers. The body, he found, produced heat that was variable, given off by the fever than by the well.

These results were very severely criticised by Dr. S. Smithson (1) who did not deny that more heat was body but thought that the loss was associated not with the fever but with the sweating which he observed, very commonly occurred with the heat desensilation.

But seeing that sweating is a very common occurrence in fever, especially in the stage of crisis, that it is by means of the perspiration that the body, both in fever, the heat, throws off, a great deal of its heat. It is quite beside the question to say that the loss is due to the sweating rather than to the fever.

The question is: Does the body in fever lose less heat or more? And whether the loss is by radiation, by conduction or by evaporation is of no consequence to the point at issue.

(2) Reactions are the proof.

The relations between the limits of the two states.

(2) From p. 187.
as to what description may be different in
health, - it is from an account of alteration in
the circulation. It is known, gives no reason
why this should be the case. It is self-evident to
see what importance should be attached to
the objection.

The second criticism is that Leyden's experiment
was in the daytime that possibly the results
might have been different at night. But as
both the well of named limbs were examined in
the daytime, there is no reason to suppose that
the relation would be different at night.

There are the observations on man which are most relied on as proving the proposition
that true heat is dissipated in from than in
health. The results are amply confirmed
by experiments on animals.

(b) Experiments on Animals.

Senator followed up the experiments
of Leyden by a series of Observations on dogs.
Taking healthy dogs, he made frequent
the injection of pus, he placed them in exactly
similar circumstances as regards food,
environment - of them, by direct calorimetric
measurement - found out the amount of heat
(1) latched by wood - "Prin" p 161 thy D. Sanderson -
"The Process of Prin" ¥ .2830.
given off by each. From these experiments he
was led to conclude that—although at the onset
of fever less heat might be eliminated, yet during
the fever, it was greatly increased—some times as
much as 70–75⁰ B. while during the decline of
the process, the increased loss was even greater.
Potential (?) got somewhat different results
from similar experiments with rabbits made
fevered by the injection of subclinical opium, in fasion
of May de. He found till the animal that the loss great
was diminished at the onset. He however, differ'd
short at this point that in this case how the heat
loss went on afterwards.

Dr. Wood of Philadelphia, made an elaborate
laborious series of experiments on dogs, which
differed from those of Senator in one important
particular. Instead of being satisfied with
an occasional observation for a short period
at a time during the day, Wood extended the
same over several hours, often 10'20 in a day.

This is obviously more certain reliable
method for it is easy to see that the heat loss
might fluctuate—and indeed it does—from
hour to hour being more in one hour than

(2) From J.C. L. 1846-3844.
another. So that the result got with one hour might be a criterion for the whole day. Whereas, when the results are taken for many hours continuously, it is much easier to get a reliable average.

There are five series of experiment. They were all carried out according to the plan. The loss from a healthy feeding dog was first measured in the Calorimetric. Then the same dog without food - then during the first day of fast induced by the injection of pus - then the second day of fast.

The accompanying table summarizes the results obtained:

<table>
<thead>
<tr>
<th>No.</th>
<th>Exp.</th>
<th>Food Day</th>
<th>Hunger Day</th>
<th>2nd First Day</th>
<th>3rd First Day</th>
<th>3rd Second Day</th>
<th>4th</th>
<th>5th</th>
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<tbody>
<tr>
<td>1</td>
<td>20/3/12</td>
<td>102-329</td>
<td>106-9329</td>
<td>17</td>
<td>17</td>
<td>162-289</td>
<td>62-95688</td>
<td>17</td>
</tr>
<tr>
<td>3</td>
<td>194</td>
<td>63-4</td>
<td>67-877</td>
<td>1744</td>
<td>1744</td>
<td>102-2</td>
<td>62-666</td>
<td>16</td>
</tr>
<tr>
<td>4</td>
<td>63-2</td>
<td>97-658</td>
<td>174</td>
<td>103-7</td>
<td>95-6902</td>
<td>16</td>
<td>16</td>
<td>105-39</td>
</tr>
</tbody>
</table>
In the first experiment, much more heat was lost in fever than during fasting, though still nearly so much as when in full diet. In the second, the dog had some meat on the hunger day too the consummation was hardly fair, but in this case, the loss in fever was just about as great for the second day, even greater than on full diet.

In the third experiment, there was no record of the discharge on full diet. But in both, though the loss on the first few days was rather less than on the hunger day, it was much greater on the second. In the fifth, the discharge on the second first day was much greater than either the food or hunger day.

So that we may fairly say that these experiments fully bear out Linder's conclusions, that the circumstances being the same, more heat is lost in fever than in health, though as novel that Linder agree, it may be often be at first, a little less.

The cannot but regret that the experiments stayed at the point they did, for as they give only the commencement of the fever they tell us nothing of what happens after.

We do not really know whether the
increased discharge which happens on the second or even first day is kept up later on, as Senator Tag, or not.

These experiments are useful as confirming the results of earlier statements, that we cannot, of course, accept them (as blood clumps) as conclusive. The conditions of heat loss in dogs—unblunted functions of the nervous system are so different, that we cannot apply them to man. They show that in animals the increased discharge is greater than during winter, though not as much as full diet.

In man, the increase is probably greater even than when full diet is taken.

The experiments show—bodily and definitely, the previous statements—that we are safe in the conclusion that in front the loss of heat is increased—probably absolutely. Certainly relatively.
The Production of Heat.

If more heat is lost, it naturally follows if the temperature rises that there is produced.

But it is not easy to prove that more is produced. There is still great difference of opinion on the point.

Two lines of inquiry have been pursued:

1. The calorimetric method.
2. Direct measurement by calorimetry.

1. Indirect Method

This part of the question is very fully and critically gone into by Dr. Burton Sanders in the paper already alluded to. The latter of the observations of Lieber, Sanders, Larral, and others analagous to them. Up to the time of the day most of the observations on this head have been those of Ruhle. His are the inconclusive results, Ruhle's results are recorded in the Medical Times.

Page 237, 287, 297, 253-331, 413 seq.

In the latter cases of Typhoid, Dysentery, Rheumatism, Pneumonia, Pneumonia, estimates the amount of loss wasted from this cause to discover the amount of heat wasted.
Sometimes the color of thea is grealer than is usually found in healthy man. Sometimes it is less. He therefore concludes that these cases in some more liecer blood in others less. But the surname of fullness are very stocious. Thus, it is the estimation of the amount of good taken. Soe the amount of secretions from other channels judged. It briefly says that the respirations are one we best quelled the skin is it is still evidently perspiring. States which are useless for finding out the amount of secretion from the organs.

The research of Leyden Walker Wood are of a very different kind.

In dealing with this violent methods, what we want to show is—"are the secretions from skin of thea more than those in healthy under the same circumstances of diet, exercise, &c."

If the amount is grealer, it is fair to assume that—in the true expenditure of metabolism necessary to produce the pleare.

Amount of secretions here lead must have been produced in the body in some, in a smaller quantity of secretions—then less heat.
The secretions partially are Carbonic acid—heat.

Walpe.
And it is obvious that it will not do truly to measure the absolute quantity of excreta without relation to other circumstances. Thus in health, much of the excreta comes from the food - the amount of nitrogen excreted being equal to that taken in - the heat production therefore which this represents comes equally from the body but from the food. It is a source of heat which is almost absent in persons on a diet of \textit{little food being taken.}

Hence, the excreta production in itself should be compared with that of a man on a diet - \textit{not of full diet.}

And it is not sufficient to state the production of excreta alone. For, so far from the nitrogen being the only source of heat - there is reason for supposing that it is not even the principal source - that the heat - 
\textit{origin of carbohydrates has a greater share.}

\textbf{(i) Excreta.}

As to whether or not there is an increase in the discharge of excreta in fever. Observers are not agreed. Dr. Sanderson in the paper previously quoted by all who deal with the subject.
undoubtedly there is more ease in former than
the conclusion that in health and in similar
circumstances, and he found his belief
observations made by Leyden, Senator, Bland,
folders.
Noting, first, the observations on man as
being the most valuable as well as that Bland after
having estimated the standard in health to
comparative discharges in cases of different kinds
of disease in which from was a symptom of fluid
considerable increase in the area.

Senators being together analyzed 13 cases of
different diseases by different observers in which
the observations were made from the beginning to
the end of the fever process with which he carefully
analyzed, having regard to the ambulatory condition
in which the patient entered the fever, he too con-
cludes that there is a great increase.

These results are corroborated by experiments
made on dogs by Senator. In them, after the canine
had been brought into a state of ambulant fever,
comparisons were made between the discharges
during two days of illness from the days of
reconvalescence. The increase in these cases too was
very remarkable.

But Senator's experiments on dogs caused a

(1) Blandon, 'On the Process of Fever.' J. 16
In these animals, the conditions of fever production are so different. The fever induced is always the same—namely, that following the injection of pus, it is quite conceivable that the increase brought about in this way might be due to other causes than the fever, for example, by irritative action of the poison itself, products in the blood, or the tissues. It would be better if these were control experiments of fever from other conditions. Then, the fever is always one of short duration, lasting only one or two days.

With the constitution is good as it goes.

In 'The Journal of Nervous and Mental Diseases,' Jan. 91, Professor Wood Marshall gives an account of investigations which appear to point somewhat in the opposite direction. In a long disease case of hepatic fever (with cholera), they found that while more were present in high fever than in low, yet that the total heat in the fever was less than normal. Here is his to be said in criteria of their results. They do not seem to have begun at the commencement of the fever. When the specimen of area is said (in the usual text) to be the highest—Let us first tell this patient—was already bailed of his space of being.

In this case, for the common bile duct was
declined. This would probably interfere to
some extent with the exaltation, at any rate
in the liver.
In the bladder, the clinical evidence occurs. The only
thing that the formation of urea in four is increased.

(2) Carbonic acid

The measurement of CO₂ being made only by
not reliable as near the result recorded concerning
it are not to satisfactory convincing.

In similar experiments with dogs (or rabbits) he found that the amount was not increased although
affinities were at work which would tend to increase
it; namely, the higher temperature of the body. But as
we have already seen, the serious objections to
these experiments, in the case of Carbonic acid there
is this further most important objection - that the
results were taken only once or twice a day - then
only for an hour each time - and with an exhalation
which fluctuates as much as Carbonic acid: it
would be impossible to tell anything from such limited
observations.

Much more important must be attacked the
results with Fretwell.

Kemp measured the quantity in four cases,
C. B. Sanderson. In the Process of Fretwell. 21
(2) Relapsing form - 178 days of incubation)

compared the amount with that for the same individual in health - the urine in question being taken at the same time. He found that there was a great increase in the carbonic acid. And from the results the
table it is very probable that in fever in general there is a great increase in the carbonic acid.

But it is well to remember that the amount of CO₂
produced is by no means a correct index of the
amount of oxidation. Many of the heat-producing
chemical changes which occur in the body are
not of the nature of oxidation at all - for example,
the splitting up of complex substances into more
simple ones. And even in complete oxidation,
carbonic acid is not the sole product. So that, while
the increase in CO₂ would tell in favor of increased
oxidation, its diminution would not necessarily imply
that there was less.

Thus as Virchow points out - it is probable
that water is formed in the body by the direct combi-
nation of hydrogen and oxygen. That this is a source
of heat.

(3) Water

The only portion of this reaction which has

(1) Extracted from "Phil. Trans. Roy. Soc.

(2) Proc. 1878, p. 394.
discovered have been those of Sebich in the experiments on dogs. He found that the amount was greatly increased.

But nothing can be inferred from them as to the part taken by excessive vibration.

The heat value represented by these various amounts of acetone has been estimated compared with those of health. Thus a quantitative result has been given. It indicates that much more heat is produced in fever than in health under the same diet. But not necessarily more than in a full diet. But that is quite beside the question.

Hence the results of the indirect method show pretty clearly that in fever more heat is produced in fever than in health under the same circumstances.

The great difference between the heat produced in fever and in health is that in health, much of the heat production comes from the food, while in fever heat comes almost entirely from the utilization of the tissues.

\(1\) B. Sanderson. On the Process of Fever. 28th. 24-28.
The richest method is necessarily less conclusive. There are so many sources of fallacy—perhaps the most important being that already noticed at
first, that the amount of chemical change which takes place is by no means the lost from
the final result of those changes. The question of CO₂ does not differ much as there are many
controversies among the times which are best
chosen by the people who know neither their habits
nor their relative proportion in health and size.

Mr. Shearmore's method is measured directly by
the calorimeter the heat produced. Such measure-
ments have been made. The best important are
those by Schwal and Wood.

2. Direct method

The very great advantage here is the recorded that
most of the observations with this method are made on
the bone animals. Dogs Drabbel. The results have
thereby to be accepted with the observations which
their implies. And thus although it is the more satisfactory
way, yet its facts can be applied (to only 5/0)
safe as they support and condense the results of clinical
study.
Senator's measurements of heat production were made at the same time as the estimation of CO₂. They already knew that this calorimetric method indicated that there was no evidence of heat production even when food was compared with variation.

Reasons have been given for regarding these experiment as unreliable. It seems likely, if not true, that the animal volunteers to them that he comes to the conclusion, (undoubtedly conclusions on the results of Leyden's experiments on the discharge of "heat") that heat production is greater, less than, and during fasting than when on full diet.

Wood emphasizes still further one of the objection to Senator's calorimetric result, namely the length of time taken for the observations.

He explains that in respect of there is a rhythm of heat production, a rhythm which differs very much from that of health that it is therefore impossible to judge of the amount of heat produced by letting the amount for an hour or ten in the twenty-four. Woods were experiments are by far the best, to measure. Careful reliable data have now been made. The human calorimeter, but by far the greatest animal calorimeter, to stop. This was indirectly by the injection of Pan-the dog was put in the calorimeter.

(1) Anderson. On the Process of Food, p. 29
(2) Forsoh. p. 166.
Every precaution taken to ensure accuracy.

Every possible source of which heat could be lost by the apparatus was taken into account. Measurements were being taken almost constantly for days. At the beginning, it was possible to tell fairly accurately the amount of heat lost by the animal. The amount produced by the apparatus were all in the same order. On the first day the animal was fed the result taken when it was on a full diet. Each day he fasted the temperatures were taken then. The next few days he was forced to fast and the temperatures taken again. Thus, it was possible to compare the heat produced under all these three conditions.

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<tr>
<th>Date</th>
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<th>Back of Day</th>
<th>First Port Day</th>
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* The dog had 13.16 rectal temperature. There was also a little elevation of temperature.
In man, the variation of the normal is much greater than in dogs, often being 6° or 7° or even more. After production increases with the length of the forearm, weight, and other factors that are true with dogs is true also much more true with man.
This table seems to indicate clearly the association offers increased production (at any rate as compared with titanium).

In 5 lb. the amount of peas is even more on full diet.
In 3 lb. there was a little diminution at the first but this was quickly made up for on the second day the increase was great. Besides the peas the amount of peas, the more heat is produced.

Also in the experiments of Wood Marshall, the peak the first, the lower area was recorded.

We must not however forget that in these cases the heat production was exceeded by during the initial stage that is, practically only for the beginning of the process. There is no guide as to what happens during later stages.

The first 10 or 20 hours high rolling continued. The lagged rise in temperature was only 3° above normal level that seems the initial with dogs.

In the lower animals, especially the small ones little dogs. But, it is common to have the normal sub-normal. The thermogenius is also below the normal level of adequacy, but it is rare in man.

These differences in the conditions of dogs between human dog should prevent hastily assuming that what happens in one necessarily happens in the other.

But since these experiments of food on the
lungs of canine form of dogs, others have been carried
out to learn which largely confirm his results
Thus, Abbott in his observations on malaria (1) found
that at the beginning of the process, the increase in
heat production was much greater than in the
normal form of dogs. Though the increase was not
maintained in the later stages of the disease, and
sometimes he found to hold good with continued fever.
Potential in calorimetric observations on the
arms of malarial children in over 100 observations in children
suffering from Malaria Pneumonia, Macciolla (2) found this increased production.

So that, whether we call the casualty direct
or indirect - pneumoniation - or malarial or not, the
evidence seems to be conclusive that in these
cases there is increased production of heat. Certainly
at the beginning of the process, doubtless if
not at all.

The question arises: From what source
does this increased production come? Is there
some activity of chemical changes this heat

(2) J. Pathol. & Journ. of the Med. Sc. 1893. p. 472
The chief only source of increased heat production? Is there some other mechanism by which correlated force can be the changed directly in appreciable amounts in heat? Of the latter, we have at present no evidence which we have abundant evidence of increased chemical activity.

Very little food is taken, yet is not, therefore to the increased combustion of well-organised foodstuffs, that the increased thermogenesis is due, we are thus compelled to the conclusion that the increased heat therein must be in the tissues themselves.

The body wastes. It does partly, undoubtedly, then want of food by the digestive assimilation, but these are not the only causes. The wasting is roughly in proportion to the length of freedom of the patient. The less from the greatest amount of wasting, is seen in pyridine.

Another cause of wasting might be from the oxidation of substances which never formed part of the body, as which was suggested, such as sugar and other unorganised substances.

Salmon's researches distinctly show that there is the existence of deviation of the birefringence of the beating
first place, while they are less fixed to the constituent—that the cause occurs.

In health he found that the relative proportion of Barium, Potassium, Sulfate, and Water was 1:2:27:1. In disease, the Potassium was about the same, the Barium increased. In cases of Rhagion Aper, Epigastria, Rheumatism, the amount of the Potassium was nearly in excess of the Barium. Hence, the source of the cause must be one or both of the elements which contain a special amount of Barium—that is, blood corpuscles or muscles.

This is supported by the observations of Vogel on cotton. If, after the colouring matter in the urine becomes strong of a more intense, more abundant.

Rheumatism again pursue another view. Remiss is that the muscles are the great source of heat.

Then the muscles are poisoned by curara. The animal plunged in a cooler medium, the temperature steadily falls. The consumption of oxygen the Shakatleri's Curare, etc. fall to lower fraction.

The reason is that the nervuous influence which should reach the muscles are stripped by the paralyzed nerve ends. The draw the influence that the share of the

themselves in the oxidative combustion, in the other -
breaking processes of the body is so great, that when
they are included a large fraction of the waste alone
remains."

Both the autogenous & Carbonaceous parts take
their share in this oxidation that leads to heat-
production, though it & Sanderson shows in his
summary of the heat values of digestible substances
that represented by the discharges Carbonic acid
and

The part with the greatest share, only a small part
of this can come from autogenous tissues, whereas
the great part comes arise from Carbonaceous ones.

It says that the only source besides albumen
is fat. Obviously, however, there are the carbon-
hydrates such for example as glycogen which is
found stored in resting muscle.

To sum up our present knowledge as the
production of heat, in brief we may say
that there can be little doubt that there
is certainly at the outset, doubtfully of
later on, an increase in the amount of
heat produced over that produced in
similar circumstances in health.

And that there is also an increase in the amount of heat dissipated.

We may even go further today that an increase in heat production is an essential factor in the process we call fever.

This factor may be absent in cases in which the temperature is high but there is fever. And on the other hand, it is possible to have the temperature drop in fever with this factor being present.
Thus we may call it 'frightened' as fairly definitely settled that the essence of fever is increased chemical change in the tissues of the body.

The real question arises, how is this increased metabolism brought about? What makes it speed?

In old times the explanation of the phenomena of fever was the subject of a controversy between
the humoralists and the stoics. The humoralists contended that the primary change was in the blood, the stoics, headed by Cullen, that it was in the nervous system.

Perhaps the greatest of the humoralists was
Poupart. He thought that fever was due to viscosity of the blood which caused it to stagnate in the retinacula vessels, thus producing the cold stage that followed.

This view was discarded for us by Leblanc who
showed in some patients in England and other countries that the fever is caused by toxins produced in the tissues. The view has been accepted as a feasible explanation.

A very old theory according to Cullen is
that the proximate cause of fever is in the culture of germs in the body of some diseases.

(Transcribed after Boole, Aph. 355)
atual. The increased action of the heart and arteries is an effort of the vis medicanis to expel the nutritive matter or to change the nature of the poison as to render it either innocuous or, at least, fit for being more easily thrown out of the body.

At the present time various explanations are advanced as to the disturbances to changes in the blood, which result in the production of the body to alter its metabolism.

Another is the direct action of the poison on the general metabolism, apart from changes in the blood.

A third ascribes the increased chemical action to changes in the nervous system.

All of these various explanations agree that the cause may be in the blood, but while some look upon the changes produced in the blood as the essential feature of the process, others consider the blood as the vehicle of communication only, and that the poison acts directly either in the interstices generally or on some part or parts of the nervous system.

It is accordingly difficult to say at this present time.
he which of these theories is the correct one. Indeed we cannot say that all are alike or being applicable for one case to another for another.

Hence, in dealing with a scientific question,

(1)

"Speaking of the vascular nervous systems,
"speaks to no greater accuracy than
"the action of the subject allows. Doubtless
"the eye of the anatomist, the vascular
"system, the nervous system are things
"apart one from the other. But to the
"physiologist, the pathologist, the practical
"physician, they are always linked.

"One cannot judge its natural reality
"functions without the other. One cannot
"be drawn out of its natural reality
"habitations. Thus play the relations, sufferings
"of disease without the other. Nor can
"be subject to the impressions of medicine
"without the other being subjected also.

"While each taken alone is vitally
"vital, both taken together exercise the
"great vital forces which move and
"inhabit the whole body."
The two systems are so closely connected with one another that in trying to explain the phenomena of man, it is almost impossible today to assign any case which one is at fault.

Dr. Alexander is today the strongest sup. of that one may call the protoplasmic theory the chief opponent of the nervous theory.

He says towards the close of his paper, in summarizing the results: "That the disorder of the protoplasm functions or of the nervous centers which produce our diseased by introducing a state which can be identified with "fatigue psychosis" - that it is possible for such a state to exist persist in the organism after the influence of the central nervous system has been withdrawn from the tissues by the severance of the spinal cord.

"That we are led back on this hypothesis that "there is from first to last a disorder of protoplasm that all the protoplasmic disorders are necessary."" Dr. Alexander wrote these words which one has been heard on the subject. It is possible that he would be willing to modify these striking conclusions.
At any rate his arguments against the nervous theory will scarcely hold their ground against whether or not we allow that there is much to be said for the theory which attributes first to direct changes in the general physi- plasm.

The statement that fever can originate and persist when the nervous system has been thrown only into action, has made on the authority of Harri who made a number of experiments on the effect of division of the spinal cord in dogs. (Sulla Teoria della febbre. Ferro 1874).

Harri found that after severance of the cord less heat was produced than before less given of that degree fever could be set up in the animal when the nervous system was thus thrown out of action and the influence from these experiments seemed to be that fever could be possible without the influence of the nervous system that such cases could only be explained by supposing that the poisoned blood acted directly on the tissues.

In the Light of more recent results would these results do not seem to be worth very much.

As the first part namely that less heat-
was produced. Now, we shall deal more fully
with that subject later on. Suffice it today
for the present that such experiments, in the
hands of different observers, have given most
variable results that the influence of the
several anal glands system was not sufficiently
taken into account. In many experiments
the healthy test production have been
found to be increased.

The second point is of more importance, but
less, namely, that fever could be set up in
the dog after section of the cord by the injection
of pure pus.

In one experiment, the temperature of the
rectum after section fell from 38.5° C to 36° C
that of the skin from 38° C to 33.5° C. After the
injection of pus the temperature rose to 38° C in the
rectum +34° C on the skin. For about 13 hrs.
then the temperature fell to 38° C. After the
section fell to 38° C and to 36° C on the skin.

In another, the temperature immediately after
section was 40.3° C in the rectum - 38° C on the
skin of the thigh. It soon fell to 38.9° C in the
rectum but in 11 hours after the injection of the pus
it had reached 40° C in the rectum whereas it-
remained for 7 hours. It then fell to 35.36°C for 5 hours more again to 30.7°C. Then, once more ran down part of a degree during 4 or 5 hours where it again reached 160°C. The it stayed for about 9 hours when the experiment closed.

The erratic character of the temperature in the second experiment lead one to suspect that other causes might have been at work than the injection of pus, it as well be taken, it is quite possible for the same phenomena to have occurred without the injection of pus at all.

And besides the fact that there was rise of temperature which by the way have passed the normal (105) in the subsequent cases sufficient to lead such an hypothesis on. A much longer number of observations would be required. The real objection is that the results were merely thermonometrical and not calorimetical. Judging of the condition of fever such thermometrical observations are of little value. They tell nothing of thermogenesis. Only of the relation between heat production and loss.
It is an interesting fact that if inflammation be caused in a joint of the nervous connections of the joint have been severed, inflammation from will still be set up.

It is evident that in such a case the disturbing element is the changed blood. That is the only channel by which the fluid producing causes could be conveyed to other parts of the body. (Except the lymphatic which in this connection might be considered as part of the vascular system).

This fact has been relied on as an argument in favour of the blood being the fluid from which the disturbance is produced.

There is this however, to be said. The blood may act only as the carrier of the various materials there is nothing to show that the real seat of the disturbance is not the general fluid -plasma or the nervous system.

The most important evidence in favour of the theory that the increased metabolism is caused by changes in the blood is furnished by the so-called spinal paralysis from want of this case.
Thus, it is well-known that in some of these
the body contains bacilli. They accompany
chemical products— that these are present before
the first is manifest—that they are rapidly
proving in numbers that the amount of poison
they produce is increasing. Their presence and
development cause all very great changes in
the blood. Such changes cannot fail to cause
their effect felt on all the tissues of the body.
It is known too, that there is a stage of local-
which only when there has been time
for the bacilli their products become sufficiently
powerful to cause symptoms of illness.
All these things create the suspicion that the
disturbed state of the blood has an important
biological effect on the tissue metabolism—on
the fever process.

In another way, the bacilli bacilli into the
blood, from developmental produce their characteristic
product. When the bacilli their products have
become powerful enough—they feel the fever. The
other symptoms begin to occur until the germs
have disappeared. It is natural suppose
that the abolition of Nitrogen. Water by the bacilli,
The presence in the blood tissues of the poison...
alluded to the substances could seriously interfere with the chemical changes in the formation of the body. This the amount of oxygen the blood can part with - the rate with which that oxygen can be taken by the tissues, the rate with which the carbonic acid can be passed back into the blood - these are processes which must be interfered with by the toxins their products which must seriously affect the tissue metabolism.

Although the mere presence of toxins which obstruct food from the tissues produce their products in the blood is not sufficient to set up the changes which produce fever. For instance it is well known that in the blood of rats there is often found in leukemia accumulates the little infectious agent - Pleuropneumonia the result whatever seems to follow.

There does not at the present time seem to be any satisfactory explanation of how changes in the blood can bring about the altered excreta - toxins how they can produce fever. But even in the absence of such we cannot altogether reject the hypothesis that the fever process may

(1) E. Coddington, trans. roy. soc. Dec. 16 1886
be caused by changes in the blood or tissues—
because these changes are of such manifest
important.

Sir Edwin Jenner says (1)

"The fact is admitted to be indisputable
that the fever following a cut in the
blood-part, do that it is certainly a
primary cause probable that a change
should be effected in that fluid before
any is effected in the nerves system
than the reverse. And there can be no
"doubt that the necessity for healthly
"condition of the blood is as essential
"for the formation of normal secretion
"as a healthy state of the nerves system.

And Kaye well argues in much the same way,

when he says (2)

"No doubt if from the nerves system is
"disturbance complicated. It must be in
"all diseases because of the internal
"connection between the blood of the nerves
"system. But is it the blood itself
"first? All the various processes of animal
"life are for the maintenance of the fluidity
"of the blood. If this is true, everything

(2)  " " Jan. 1853  p. 8"
"Languishes. It is the incurable condition of the blood which facilitates the organism. Even local or minor changes in the organs themselves, and the point of reference to the intake of blood being the process of respiration by acting on the central nervous system.

It is very easy to understand how any part of the nervous system (including such as may be concerned with production or loss of regulation of heat) might be disturbed by such profound alterations as are those to which place in many fever that is extremely difficult to explain the first brought about by the introduction of deep poison and such diseases as acute and relapsing fever without supposing that the death of the blood has much to do with the causation of the condition.

It seems more than likely that changes in the blood are very frequently the primary disturbing agent, that the alterations in the nervous system are only secondary to these.
The Animal Theory of Fever.

But however doubtful it may be that fever may be set up by changes in the blood or in the general fluid plasma, there can be no doubt that fever may be caused by the direct action of the nervous system.

If a theory of the febrile process is to be formed, it must be based upon the relation between the nervous system and processes of nutrition, especially the latter. (1)

The nervous theory of fever is best a nervous theory, for we find Cullen writing: (2)

"Upon the theory the doctrine of fever is altogether different. The causes are external and applied to the nervous system, which diminishes the energy of the brain, thereby producing a debility in the action of the functions of the body, particularly in the action of the peripheral vessels. Such debility is at the same time the cause of the animal suffering from the cold. This debility proves an "indirect stimulus to the vascular system." Hence, by the cultivation of the cold stage.

The action of the heart and breathing is increased, and continues to untile it has had the effect of restoring the energy of the brain, of leading this energy to the glandular system, of restoring, therefore, their action thereof, especially increasing the plasma affecting them; upon the moment of which the relaxation of sweat, the withdrawal of the relaxation of secretions takes place.

This theory still holds its former though stated somewhat differently in the retention theory of Feurthe theory.

But the real originator of the development of the retention theory in recent years was Michel - whose classical definition - found in all the books.

"Thus consists essentially in elevation of temperature which causative from an increase to some change appears to have its immediate cause in alteration of the nervous system."

And there is nothing inherently different in the theory. For what we have been for essentially phylogenetic, devolution, and later on, the
issues of the body. These can be in doubt about the control of the nervous system over the metabolism. That diseases are affected in the nervous system may produce great changes in the metabolism. And if this be true, it is not difficult to imagine that the changes may be of such a kind as to be of the phenomena of fever.

A great deal of evidence in connection with this is furnished by the results following division of nerves. by neuralgic herpes, lichen planus, produced by lesions of diseases of nerves. It is not necessary to go into all the details of these things, but for the sake of this discussion it may be well to look at the whole for a moment-attention some instances of changes in the nervous system producing changes in the tissue metabolism.

Attention, e.g., is called to the fact that the 4th ventricle, which contains diabetes, the only satisfactorily explained effect of the phenomena of diabetes in the glycogen metabolism of the liver, is the result of direct action of the nervous system.

In the American lectures on the pathology and physiology of rheumatism, 1886, D. M. H. Bachman draws attention to the fact that diseases of the nervous system may cause changes in the metabolism.

(1) Mosher's Physiology, p. 4460 (2) p. 390
(3) Med. Jour. 1886, p. 574-5
He quotes from a book by Mitchell, containing the
abuse of cases of painful long continued swelling
of various joints, leading to partial paraly.

He quotes also from St. Lucia, accounts
of similar cases, following especially injuries
of the brachial or sciatic nerves. He himself relates
3 cases. One of injury to the brachial plexus.—
development of the lower extremities—loss of sensation
in the foot with important reflex changes.

Another case of injury to the sciatic nerve,
resulting in an almost certain flaccid paralysis of the limbs.

He also notices Charcot's cases of joint affection
following meningo-encephalitis.

It seems very clear that injuries the cases of
injuries may cause real alterations in the body
resulting in paralysis.

In a case which came under my own ob-
servation of a man suffering from an unusual form
of spinal tuberculosis, the hands and feet
contracted (actually, then ceased to be)—some of
them finally coming off altogether.

From the last account of Dr. Pitman, above, it
is

(2) From "Injuries of Nerves," 1872.
Contracts, it must also be noticed that changes in its metabolism.

In a cold-blooded animal, heat-increases tend to diminish the metabolism. In a warm-blooded animal, the reverse is the case. But paralyze the voluntary nerve and add curare, the animal acts like a cold-blooded one. Less carbonic acid is given off. Less oxygen is taken in. On the application of cold, it is necessary to suppose that the metabolism of the muscles is lessen, the content of the blood oxygen.

Frankly then, that such conclusion does exist, it is an easy step to suppose that the changes in the metabolism are such as to cause fever.

The evidence that the nervous system is principally concerned in the causation of the process is thus far - *Clinical Experimental.*

*Clinical Evidence that fever may be produced by changes in the nervous system.*

In health, the temperature of the body is nearly constant. Whatever the accidental causes of great production, the loss is always such that an

There must be in the body some mechanism which controls this, and the temperature is so constant, the varying changes do rapidly tend to be compensated for, that it is difficult to say in what extent this mechanism does not largely depend on the temperature being either of constant or variable. The mechanism is changed.

The cutaneous circulation is constantly varying. Sometimes the vessels are constricted, sometimes dilated. The patient's face flushes. Some hour his face is hot, some hour it is blanching. The cutaneous vessels are contracted in an irregular manner, showing that the nervous mechanism which provides for the loss of heat from the skin is disturbed. It is evident that there is a nerves element in the process.

There are many things which indicate that the nervous system is essentially at fault. They are indicible that hypoglycaemia is especially common in these diseases in which the nervous system is specially involved—i.e., stones, beds, central nervous system diseases of the spinal cord. It is also common in acute nephritis, a disease which is caused by some 

(2) Lehmann, 'Nervous System.'
of nervous origin. peculiar: the occurrence of hypertonia is always preceded by nervous epiphora. Thus in acute rheumatism, last only do the pains in the joint, frequently disappear before the onset of the high degree, but the patient is usually restless - even delirious or semicomatose.

In one of my own cases, let 10.33 years ago, with acute rheumatism, had back pains in the chest, mandible joints (followed by Pneumonia at the base of the right lung) then by meningitis for 60 days. On the morning of the 5th day when I called his pains had all gone, but he was very restless and delirious. His temperature in the arillae was 102.4°F. At 26 clock to the afternoon it had gone up to 105°F. He was picking the bedclothes, delirious taken. His tongue was packed with He was placed in an ice pack at 3:40 am to reduce the temperature in the axilla temperature fell to 105°F. At 4:20 it was 103°F, 5:40 it was 101°F at 7:30 98°F. When the ice was removed, the temperature kept up for several days but never again was higher than 102°F. The lad got quite well.

This case illustrates another point which would occur to indicate the close connection there is between the nervous agenesia.
namely that the application of cold has a good effect on these cases of hyposthenia. It seems as though the cold acted not only directly by ab-
tracting heat, but also indirectly by acting on the nervous system that the heat-production tissue metabolism was diminished.

Evidence of the same kind is furnished by other antipyrinics—such as antipyrin.

Here is a careful study of the effects of antipyrin to these antipyrinics after noticing evidence exper-
imental. Clinical obtained both by directly that the con clusion that (except in toxic doses) antipyrin has little effect on the blood itself or the circulation. It shows the general influence of the antipyrin the production of heat, this being evidenced by diminished respiration. That it has a decided effect on the nervous system, diminishing reflex activity by depressing the sensory and motor the cord. The latter 

...But all this evidence is insufficient. There is enough more direct that is more direct and useful. For many cases of injuries, diseases of the nervous system have been recorded in which these have produced disorders of the body heat.

(1) From its Pathology and Treatment By Antipyrin.

By A. H. Hare, M.D., Boston, Massachusetts 1874, p. 38.)
The following — which is at the present time
under my observation, is a case in point.

Mr. a man 22 years of age — was admitted
into the St. John's field surgery on the evening of
February 6th 1872. During the afternoon he had
been playing football which running with
the ball, he was seized thrown to the ground
his head being doubled on his chest. Two or three
seconds after the loss of their balance in this position he
fell a crack in the neck immediately lost the
power of move the part below. He had also, all sense of
feeling.

On examination, there was found the complete
paralysis, sensory paralysis from the neck downwards
the Brachial pleuris being involved. There seemed to
be a little feeling over the distribution of the 6th and
certain bones but it was lost almost.

All the respiratory muscles except the diaphragm
appeared to be paralyzed of respiration seemed to be
carried on only through the agency of the diaphragm.

On putting the finger into the mouth a hard
dothing was felt projecting into the pharynx of
was seen to consist of the bodies of the 4th, 5th, 6th, 7th
Cervical vertebra. Capitans was thought 1082 fell
on the lepisode of the upper jaw of the projection.
The temperature charts are given below.

The temperature varied very much - some times being considerably out of normal at other times very high - the changes often taking place in the course of a very few hours.

As far as could be judged - the course of the temperature was not determined by external conditions. The bed was always kept as nearly as possible at the same temperature the bed covering did not appreciably alter this warmer.

The treatment consisted in elevating the head, the head being lower than the body. The legs weighted.

Up to the present time (April 22nd) no check change has taken place in the patient's condition.

On March 8th, 3 red lines developed in the middle of March (11th, 15th) he had two small red spots on the shoulders, which quickly healed. About this time the left leg seemed to the left side of the leg (arm body), became edematous and the adrena is still present. Sensation has returned in the left hand with some movement in the left arm.
**Name:** J.H.  
**Age:** 22  

| DAY OF DISEASE | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15-16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 |
|----------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| DUR. | 10° | 3° | 3° | 6° | 6° | 6° | 7° | 7° | 7° | 7° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° | 6° |
| RESP. | 40 | 24 | 22 | 18 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| NP. | 24 | 22 | 18 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |

**Remarks:** Observations taken at A.M. and P.M. For Memoranda of Treatment, see back of chart.
In the Medical Times of 1837 (p. 285), Dr. John H. Jones, in dealing with the question of the influence of nerve stimulants on fever, tells of the case of a gentleman with a weak nervous system (probably due to strain of nerves), in whom a very slight fever agitation would produce fever lasting 20 years.

He remarks as that mental depression remained prominent, the liability to attack from fever, following from the same cause, that any severe attack of the mind, such as grief or anger, is very likely to follow an attack of intermittent fever.

He also adds a list of cases in which injurious diseases of the nerves of the skin produced alteration in temperature.

There are 3 cases of injury to the cervical cord due to disease—1 recorded by R. W. E. Godfrey, F. F. C., and S. B. Biddle—the maximum temperature ranging from 107° to 104°. One of injury to the back, followed by broncho-pneumonia (Child's case) the temperature reaching 102°. One of injury to the middle of the back, these being also lethargic, mentioned by Dana.

Two cases of fracture of the skull—1 with concussion of the brain (Biddle)—the temperature reaching 107°. The other—death of the brain (Wald)—the temperature being 109°.
In addition to these, there are 4 cases of injury to the cervical part of the cord, in which the temperature has not been normal—two recorded by Mr. Hutchinson—ejecting to the cervical spine with paralysis. The temperature being 94.4°F. Another by long stiff fracture of the lower part of the 6th cervical—the temperature being 92.3°F. Of physicians Mr. 76°F. The remaining two by fracture, the temperature in one being 92.3°F. In the other 86.36°F.

With regard to supporting further evidence of the same kind, in addition to cases mentioned above there are 16 case by Mr. Hutchinson of fracture of the 6th cervical vertebra, with concussion of the cord. The temperature reaching 101°F. Another case of Hadden's of fracture of the 6th cervical vertebra with concussion of the cord at that level—the temperature getting as low as 96.7°F. The third by Churchill ill-fracture of the 5th cervical—the temperature getting as high as 107°F.

But to give the best clinical evidence is accumulated by

(3) Dr. Willmott in a paper entitled "The Theory of Heat-Cure from a Clinical Point of View."

He then brings together a large number of cases in which the most probable explanation of the
disturbance of temperature is alteration in our rest.

It carefully excludes from his list every case in which another cause could be alleged—such, for example, as those in which internal bleeding occurred.

In detail are the following cases—

Two of lesions affecting the central cord—the temperature reaching 103°1 to 101.4° (in the case of Dr. Perry, Beechill).

Five of lesions of the Brain—the temperature reaching 103°1 to 100.8°, 101.4°, 101°1 to 100.4° (in the case of Dr. Beechill, Dr. Ferguson, Dr. Pierson, Dr. Ridge—Jones, H. Beever).

Eight of Central Hemorrhages—the temperature reaching 101.4° to 100.2° (in the case of 100°7, 100°6, 100°7, 102°7, 106°4, and 105°7 (in the case of Dr. Ferguson, Hall).

Six of Hemorrhages into the Cere-temperature reaching 101°2, 102.2°, 102.4° (in the case of Alexander, Hill's, Thr.cked).

Two of Central Autolysis—the temperature being 105.2° to 101°7 (in the case of Hill's).

Eight of degenerative changes in the Brain—temperature 101°7, 108°7, 107°, 107°, 106°2°, 106°2°, 102°7, 105°7 (in the case of Alexander, Hill's, Thr.cked).
One of Eberhardiana. In the cases the temperature
always rose to 103.2°F to 104.2°F (illness).

One of Obena have been cases in which no
change was found post-mortem. In one of these
there was hypertension in a young child (Taylor.

In both the temperature rose at times during
many years (postnatal). The 4th case was seen
by J. L. Kedans.

Several cases of hysterical hypsystole.
especially one recorded by J. L. Kedans in
which the temperature rose to 128°F.

The case of Injury to the Brain following fracture
of the Occipital bone in a child (Case of Dr. Davies Collie).
The temperature rose to 102°F.

Two cases of Injury to the Spinal cord already
mentioned.

In addition, Dr. W. S. Pearl's cases of nerve affection
accompanied by fall of temperature.

One of Cauda of the Brain. This is the one case
described above as having a temperature 103°F
as far as we could tell very low in this instance as well as the Brain.

Many cases of Central localization were on
record, but in these the fall seems to be
more pronounced.
In addition to these there are cases of degenerative changes in the brain, including disease of the spinal injury in tabes dorsalis.  

Dr. Wood has also collected a list, in which besides many of the above, we find —  

A case of hemorrhage confined to the optic *Kalamus* recorded by Denny, in which the temperature registered from 32.9° to 37.3° C.  

Cases of hemorrhage limited to the brain.  

(a) Cases in which there was rise of temperature recorded by Kurney, Alexander Johnson, Lepere, Prince Videaux.  

(b) Others in which the temperature was normal or subnormal. Recorded by Wethered, Storey, H. Brown, J. Nobesano, and Brown.  

Besides the cases here noted are others which will be seen later. These will suffice to show conclusively that first may result directly from injury or disease of the central nervous system.

(c) Forsr. p. 153.
Experimental Evidence that pyraemic shock produced by changes in the nervous system.

The clinical evidence, though very strong, becomes stronger when, as is the fact, it is supported by experiment.

The clinical evidence is valuable because delay with man has one great drawback. It is impossible to ascribe with clinical results as with experimental. And, besides, one cannot tell from these records of temperature whether the changes are due to alterations in heat-production or in heat-utilization. The fact that results got from the experimental are carefully measured in the calorimetric, great as are the possible fallacies with this method, enables these experiments of some much more value. And though too may not reason directly in the case of the nervous system from dog to rabbit to man—yet then the experimental results corroborate the clinical ones, the evidence becomes very strong indeed.

Superaclu revealed that section between the pons and medulla in the rabbit was followed by
rise of temperature. His statements were subsequently confirmed by Cawdrey & Buckle. The latter, article 2 stated that the rise was from 37\deg F.

There seem to have been the most reliable data in the period until 1880 when Wood examined his series. He also confirmed these but went further. Besides finding that he could in dogs produce fever without setting up various changes in the brain, he, among others, - -
- population results. But these we shall look more fully into dealing with the position of question of the position of the part of the brain concerned with heat production. In the meanwhile we may bet it for granted that the nervous system is primarily associated with the causation of both

The real question comes -

"Which part of the nervous system is it which is concerned?"

Held in brain - Wiers contend that all the changes are to be explained by the action of the Vaso - itor currents, which from injury or disease are so affected that they fail to control heat loss as they should.

Others again, such as Wood, Hale 

\[1\] Cited by H. Jones, [ed. Jour. Phys. 177, p. 67];
\[2\] Simple of [ed. Jour. Phys. 188, p. 67];
\[3\] Simple of [ed. Jour. Phys. 188, p. 67];
\[4\] Simple of [ed. Jour. Phys. 188, p. 67];
are certain that, in addition to the vascular centres there is a special centre or centres which control or mediate over the production of heat. Though they differ as to the exact position significance of each centre or centres.

Vascular centres.

If fever is produced through the action of the vascular apparatus merely, then it must act in one of three ways—

1. By acting on the superficial vessels that they contract—thus injuring the skin and the circulation rising on account of retention.

2. By acting on the vessels which supply the musculature that they dilate—thus increased strain is encouraged.

As to the first—that fever is due to contractile of the superficial vessels, we have already seen that such a view is untenable—that Sahara fever being retained in the body, it is given off in great abundance. Therefore, therefore, dismiss this part of the theory.

The second is much more plausible. Fevers more detailed examination, it is that the vascular centres are in such a condition that the blood...
going to the muscles are dilated that therefore the metabolism is encouraged.

It seems only reasonable to suppose that if these vessels are dilated they will carry with them more blood - more oxygen - more opportunity. Therefore, for a chemical change to occur. And this opportunity will be greater because not only is there more substance brought into tissues, but the current being obtained from the dilation, the parts are brought more thoroughly in contact with one another.

Hence, one would expect that although each part of the blood is less thoroughly oxidised, the total amount of metabolism would be increased, that is, more heat would be produced.

Such seems a very plausible explanation. There are not wanting experiments which seem to support.

Thus division of the cervical sympatheic in the rabbit is followed by dilatation of the vessels of the ear on that side, the temperature may rise more than a degree higher than that of the other ear.

Conversely, division of the sciatic nerve is followed by a temporary dilatation which is soon replaced by constriction. The foot becomes paler and colder than that of the other side.

(1) \textit{Physiol. Rev.} 1907, p. 203  
(2) \textit{Ibid.} p. 183  
(3) \textit{Ibid.} p. 193
These results are confirmed by Stein-Lehar—Riegel of Hanover (1).

Again: The phenomenon which follows section of the cord occurs to be easily explained by this method. In Schulz's experiment falls it is due to the fact that the vasomotor centre is cut off from the vessels it controls. The arteries of the skin dilate, much heat is dissipated.

Then the temperature rises, vessels of the muscles which are also dilated, allow no heat to rise heat production to occur that it may be more than can be balanced, the loss.

Such is the explanation favoured by Mr. Hutchinson's also by Professor Arrhenius (2).

Now it is obvious that the deposit of oxygen and other materials for tissue change, must necessarily obviously affect the amount of metabolism that occurs place. If that be insufficient, the metabolism cannot be do great— if it be excessive there is more chance that these will be increased tissue change.

But, there is no reason to suppose that this increased change— will of necessity take place, unless some- thing takes place to enable the muscle take a form.

(1) London Medial Rep. III. 366
(2) Hutchinson. Proc. R. Soc. 87, 1922.
(3) Hutchinson Proc. R. Soc. 87, 1922.
- age of its opportunity. Dr. Lecato, in fact, had

the matter very keenly

early.

"Changes in the absorption of temperature may

result from changes in the respiration of

the tissues; but I know of nothing that justifies

us in straight way assuming that such

changes affect thermogenesis. The mere

flushing of a muscle with blood need not

increase the metabolism of the muscle

outstanding unless the latter is oscillatory

stimulated by functional activity - unless it

is excited at the right advantage to the

opportunity for assimilation which are

afforded it. Cut off the circulation of the

muscle by clamping off may cause the

arterial blood to rush through its vessels

without appreciably increasing its oxidative

metabolism."

And there are many reasons for hesitation

to accept the theory.

Bernard & Knoeck found that after dividing

the central sympathetic in the neck, the blood

tension of the car on that side remained higher after

increased muscularly had disappeared.

(1) The Nature of Force p. 37

(2) Foot's Physiology p. 436
Bernard also noticed that after division of the cervical sympathetic, manipulation of the central end of the divided auricular nerve, being enough to cause pain on the other side (on which the sympathetic was intact) a fall of temperature (even 3°F) without pallor, although the temperature was increased in other parts of the body.

Besides, manipulation of a part-nerve going to a part will cause a rise of temperature even if the blood supply be cut off. Thus ending fibres shows that the temperature rose in the submaxillary gland after manipulation of the Chorda Tympani, even after the vessels going to the gland had been ligatured.

These considerations induce us to think that although dilatation of muscular vessels and increased metabolism go together, yet that the two processes are quite independent of one another, as caused by different agencies.

The changes which follow section of the spinal cord, not are capable of another explanation, although undoubtedly the vascular system is modified. We shall see this later on.

It is known that increased production of heat follows section between the Spinal Medullae as the division is above the interspinal centres.

(1) Foster's Physiology, p. 436.
(2)
would seem as though they could have nothing to do with the phenomenon.

But Heidenhain (Vesalii Ossis) still held the vasomotor theory. He explains this occurrence by suggesting that it is due to excitation of the vasomotor centers.

They formed their belief on experiments made by Bech of which he noticed that by puncturing and irritating the vasomotor center in the medulla, he got the same results. That is, therefore, the cause of the increased production was due to this excitation, but to excitation of fibers passing from an inhibitory heat center higher in the brain, as Heidenhain said.

Wood strongly opposes Heidenhain's views. He shows that these are another signs of inhibition present, that the rise in temperature does not reach its height immediately after the needles are introduced (as would be expected were it due to excitation) - half an hour later. Also, that by slightly warming the toes therapeutically, as he supposed irritating fibers from a heat inhibitory center, without in any way exciting the vasomotor center, he could get the dilation reaction in heat production. It is impossible, therefore, in the face of such facts, to keep up any belief in Heidenhain's hypothesis.

(c) (2) in Wood (Foot p. 53), Hub White (Vesalii Ossis, p. 76) and Heidenhain (Vesalii Ossis, Foot p. 63).
According to various observations (of the LLacunae) openings in the lining of the brain, which are called "LLacunae," as well as other openings in the brain, the LLacunae are caused by fluid from the blood vessels to the brain that has been absorbed and has led to the development of the LLacunae. The LLacunae are filled with a fluid that is found in the brain and that is not able to escape, leading to the development of the LLacunae.
There is just as much reason for supposing that the heat function has some part of the brain to prescribe over it, as that the rhythm function has.

As well in preparing the evidence on this question, with the experimental as with the case of the clinical.

**Experimental Evidence as the evidence of a center or centers concerned with the production of heat.**

This points to conclusions which are more definite than those derived from a study of cases. For example, therefore, see what these conclusions are when compare them with the clinical records of individual cases, one bear and the other.

The experimental evidence very clearly the evidence of a part of the brain at any rate, to dogs and rats, which seems to be concerned with heat-production, which the fullest discussion of the question is found in Wood's memoir. He not only keeps Jennings' results, he coordinates all the leading conclusions previous investigators but he carries out a real—many experiments of his own, nearly all on dogs. They clearly many doubtful points.
The only. instance case of high temperature after injury to the spinal cord. His reflexes on the section of the cord in rabbit seem. Leave at the writing growing.

Numerous instances succeeded him. It was soon found that the operation was followed by a fall of temperature. Thus if the surrounding air were colder than the body, the temperature continued to fall until death.

If, however, the animal were wrapped in lead to the surrounding temperature kept up, the fall was at temporary. The rise occurred which ceased the temperature above normal.

Wood noticed that the larger the animal, the more likely was this to occur.

The question then arose: "What is the reason of the rise?" It is obvious that it is not the decrease in the production of heat. Or diminution of the temperature. Section the cord at different levels in dogs, a calorigraphic folliculate the production of heat. Wood found that section was invariably followed by a decided increase in the temperature. That the amount of the increase was in direct proportion to the keenness of the section to the brain.

It was easy to pass on to the next day. woods (1) Form p. 36.
What was generally thought, that the increase in the dissipation was due to Dase in body paralysis—the general centre in the medulla being ceased. The increase gradually diminished 1100 became densityless—tissue would only be subjected with a cooling body.

As to the production of heat, he found that at first this was less than before. The decrease production he attributed to the Macomber paralysis:

(A) Directly—because it diminished the temperature of the body, the cooler the body got, the less chemical action would take place in it.

(B) Directly—also in this way. The general Dase in body paralysis would cause a sluggishness in the blood current in all parts of the body, this would predispose to lessened chemical activity.

But it is not quite certain that the second event would take place for although with a quickened circulation, a more active interchange would seem between the tissues the blood—jet, their not being oblique an amount of blood passing through the constricted arteries. If going through too unrequital, it is easy to think that the total amount of change might be made with.

Dr. Ford—p. 165 dec. 20.
the sluggish blood current in the dilated vessels, each particle then being more fully for a longer time in contact with the tissues. So that possibly the irritative action of the vasodilator paralysis is the one that acts.

The thin effect of the coatings of the body from increased dissipation passed off, there seems to be a tendency towards increased production - especially in target animals.

The inference naturally follows that, in addition to the influence which superintends heat loss (respiration applied), there is no other which tends towards increased production.

To get at this, the first thing was to eliminate the vasodilator centre, the effect on the production being real.

To do this Wood repeated the experiment of Denjunkow. Heidenhain & Pittman. He divided the medulla from the first spina section of the dog's spinal column, tried the effect of stimulation of a sensor nerve. His results were the same as those for the stimulation caused a rise in the blood pressure, just as if the operation had been done. This proves that the vasodilator centre could rise higher than the vasodilatory junction.

*(1) W. W. Physiology, p. 208.
(2) W. W. Physiol. p. 52.*
Surgery to the medulla had just the same effect as on the temperature as injury to the cord except that the results were even more marked.

Doroshevich had already stated that when he divided the medulla from the spinal cord there was an immediate strong marked rise of temperature.

But his experiment had been contradicted by Huxley who, in dividing similar ligaments of the spinal cord, observed results sometimes the temperature rose, sometimes it fell. Food suggested that the reason why these observers did not confirm his previous work was that rabbits—unlike the animals used by Huxley—such small animals they may not with a central decompression be so delicately prepared as to do delicate an experiment—dismembering the forebrain without injuring the medulla thereby causing the medullary paralysis anticipated to follow.

Therefore used larger animals—dogs—hippokonts on their methods of operating. Found in a large number of instances that in every case (except when the mass and its centres were implicated by cancerous growth as pressure of blood clot) that the temperature did rise as Schlesching said.

He controlled the experiment by seeing that stimulation of accessory nerve caused rise of
Blood pressure—proving that the Vasomotor Centre remained intact.

It failed to get the rise of temperature in rabbits, as did Bruch & Jahn—For the same reason, probably namely, that the Vasomotor Centres were injured.

Whenever the Medulla was seriously disturbed, there was a fall of temperature—decreased production increased loss of heat. And in all other cases, when there was a rise of temperature, it was invariably followed by increased production of heat—this increased production of heat was accompanied by increased dissipation—this loss did usually keep pace with the production of heat, temperature therefore rising.

It was not difficult to explain the increased production of heat. The Vasomotor Centres being intact, it would gradually try to come back at the rise of temperature, following increased production—the loss, therefore, would be increased in accordance with the increased production.

The explanation of the increased production was not too easy.

Heidenhain—Bruch & Jahn—said that it was the localization of the Vasomotor Centres—that we have already seen reasons for thinking that such could be the true explanation of blood flow but the acceptance of their explanation offered by Fraenkel—so that there must be in the brain at a point higher

(1) Pp. 33 Col. 2.
than the upper border of the medulla, a center or centers whose function it was to initiate the production of heat. That, therefore, the increased production following action was due to increase of nerve fibres going from that center the tissues, nothing then being present to restrain the chemical activity.

Wool then, that is prove indirectly the existence of such center or centers. Taking advantage of Heidenhain's discovery that excitation of a peripheral nerve was followed, not only by rise of blood pressure, but also by fall of temperature, an experiment corroborated by Heidel thicker— & he repeated it—found that, though the excitation did fall too fully, yet that while the blood pressure was high, there was at first a slight increase of temperature. This, however, soon gave way, & was followed by a fall which continued some time after the blood pressure had fallen to normal.

These experiments then dispelled Heidenhain's theory that the fall in the temperature was due to evaporation of the vascular centers, as demonstrated by the rise in the blood pressure. Further, showed that the temperature was independent of the state of the circulation—this being measured by the

(1) "Wood—Proc. p. 86
(2) " " p. 86-7
arterial pressure.

And content with this, Wood repeated the experiment—after division of the roots from the cranium. The result was that the fall in temperature did not occur, though the vaso-motor centres remained uninjured. The blood pressure was as usual.

And, in addition, he found that the denervation of the experiment, which were intended to prove the contrary, really corroborated his own.

The conclusion he drew from such records seemed to be that the fall in temperature was produced by action on some centre or centres situated in or above the tons.

So far all had been plain sailing, one could look calmly at the results. But when Wood went further, tried to demonstrate more exactly the position of the centres, it was all toays to localize them.

By inspecting carotic bodies into the brain, turning away portions of brain tissue by washings or washing them away with water, he tried to localize the centres. But it is sufficient only to mention these two methods. He sceptical about conclusions that are drawn from them, salaciously.

All the cases far too much tissue was destroyed to lead to any definite results. Thus, in one case, in
which the operator tried to destroy the Pois by injecting strong Ammonia, the Cerebellum was very quickly destroyed as well as the upper portion of the Pois it is true that in another injection of Ammonia acid there was complete destruction of the left Cerebellar lobe. Evidence that the upper superficial portion of the Pois.

In an attempt to destroy only the right's area' Caudate area posterior to the Cerebral cortex in the dog there was also identified with the part mapped out by Forrin for the lateral areas for the other side. We find that the cerebral flexure had made a curved through the grey matter about 1/3 inch indicating traversing the outer part of the Cerebral cortex of the 3rd and 4th convolutions on one side. On the other, a wound posterior to the Sulcus, involving the whole brain beyond the first convolution reaching in depth nearly to the Ventricles.

In another in which the brain had been twisted away freely through cephalic openings, there was a very large wound involving the 1st, 2nd, 3rd and 4th convolutions running across the Sulcus Crusading tending to the Ventricles. On the other side was a wound about 1/3 inch posterior to the Sulcus Crusading involving the 1st, 2nd, 3rd convolutions of

(1) from 1/97.
(2) 1/98.
(3) 1/99.
Attending to the ventricles, &c. &c. &c. In
several cases one of the experiments does
the lesion seem to be even fairly limited to the
region in question.

The results following each course methods and
therefore, be accepted with caution.

Still they may be taken as far as they go to so
far as they corroborate previous experiments, and
they certainly do seem to warrant conclusions come
to by others.

Thus Pauwels found a consequence
of destroying this area in dog, that the temperature
up of the opposite hemisphere increased, whereas
the difference
between the two sides of the brain many degrees
larger. Section of other parts of the brain
had no effect at all.

Professor Hitzig too got nearly the same result.
Experiments were done in December. In 14
Hitzig's region was destroyed the 13 the heat production
was decidedly increased (the 14th was easily explained
away). In the remaining 6, the region was likewise
injured, while other parts suffered the temperature
remained unaltered.

In the table distances of lesion of the area by

1. From p. 107
2. 9.8
3. 139
call, the heat production was diminished. All these results are so much alike that we are bound to conclude that Helbig's region in dogs must have some intimate connection with the inhibition of heat production.

Whether there be then a special centre for the parasympathetic or whether it be oblique to this elsewhere (as the Purys as Wood suggests) or whether it be a muscular inhibitory centre - we cannot decide.

It is not unreasonable to suppose that the main centre should be close to those which produce over the muscle functions - the relations between the two being so intimate. This would make one suspect that the main centre must be in the cortex.

As to whether the centre is muscular, parasympathetic or heat inhibitory - it seems much more likely that it is the latter. If the sympathetic Nasi be divided in anaesthetized dogs the sensitive nerve irritated the blood pressure will rise perceptibly. Irritation of the sensitive or Helbig's area in dogs produces no effect on the blood pressure. The result is just the same when the sensitive nerve is irritated. The sympathetic Nasi divided.

Now as the muscles contain about 74 of the blood of the body any centre preceding over the bloodstream

\textsuperscript{1}(Wood: From p 153)
The muscles would be densely affected in these cases, corresponding results would follow.

But as no effect follows the destruction of this area in dogs, indeed, follows cessation of the

Nervs from the Medulla, it is difficult to believe that

any important vascular or other centre can be above this

Hence the area in question is in all probability but a

vascular process. But heat-inhibitory.

In his these experiments others have been

madly Alkoren Hales in Dublin, by 84 in

America 87 Hale Deitch in England.

Dr. Alkoren Hales (1) found that elevation of the

corpus striatum in rabbits was always followed

by rise of temperature. The elevation continuing for

many hours. Along with the amount of carbonic acid

given off by liver taken in where increased.

And this, without any elevation of the body function

without apparently influencing in any way the

vasomotor apparatus.

Dr. Hales (knew in 1899) refers to fraud of Dr. Hales by

assaying the same thing.

He also put on record an account of his own

experiments in rabbits. He allowed for the local

(1) Pflüger's Archiv, 1835. Kundert, 58 Calend. Physiol. 79;

Janin, 1 of 1893; Hale (knew in 1899) G. in the

Autonantiurnal Journal 1890 II, p. 473.
fluctuations of temperature in these animals. For the influence of the ether – the effect of which the surgeon before hand, he had, had,lodged experiments in which the laminae ventriculus alone was injured. His procedure consisted of glancing a hollow needle down to the base of the brain, near the lower end, and a wire could be pushed out from a tube in the tissue portions of his vascular tissue could be injured in one eye.

But it had previously noticed that it was not uncommon for the wire to be in front of the corpus striatum or the thalamus that was followed by rise of temperature. But it was not rare. Results painted various.

In his cases the wire in the laminae alone was plunged up. So of the 14 only did the temperature rise higher than 103°F (the normal being 98-100°F). In 2 out of the 14 the corpus striatum was touched. If the climbing up, the developed central areas of the others showed a drop in the 103°F to 100°F, a rise 80 slight that it might easily be due to the tenacious causes.

While therefore, concluded that injury to the wire in the laminae alone did not affect the temperature unless the ganglia themselves were touched. Another was the more one of this because in the 3 cases.

1) British med. Jan 1891 p. 1401
Distance by which the temperature rose after injury to the white matter alone, the lesions were seen in the ganglia that they could scarcely escape.

In 23 experiments, the corpus striatum was the part mainly affected. In 2, the temperature reached 106-108° F. In 7, 106° F. or over. In 11, 105° F. or over. If the lesion was in 4, there was a slight rise in 3, a slight fall in 2 (10° F. to 2° F. only). In both cases the lesion was an infracted one. The duration of the rise averaged about 58 hours. If a fresh hemorhage occurred, there was a secondary rise. If the hemorrhage happened to be large one, the shock was sufficient to make the temperature fall before death.

In 9 cases, the thalamus was injured in all the temperature rose. In 1, it reached 105.6° F. In another, 105.8°. In all but 1, over 105° F in that one the injury was severe the shock occurred.

On the whole the rise was not great after injury to the corpus striatum alone. It usually reached the highest point in 60-70 hours and aged here, on the average, about 42 hours.

The conclusion to be drawn from these experiments seems to be that the corpus striatum...
Hoátes asked: the Opia Stalums have an important relation to heat-production, probably depending on heat-fusion.

And the conclusions are confirmed by Otto Pavlovski. He not only get gelatin-like results but discovered that if the corpora striata had been removed it was impossible to produce fever by injecting pure fluid. (1)

Otto's experiments were ecolonialical of the fever, more distinct than literal. (2)

Perhaps one might tell except that to vary definite statement as to which if the red or the white or grey matter had most to do with the results. The rabbit's brain is very small of the basal ganglia dominate that it was the exceedingly difficult to tell which suffered most after such injuries had been inflicted-by such means as were used.

Now many of these results support the theory advanced by D. Macalister in the fall.

Seems necessary therefore to mention that Young D. Macalister suggested that in the central nervous system were three separate facts—which

1. International Journal, 1890, p. 473
Supra-integrated these separate functions. One
fact-controlled thermogeny is - metabolic - control.
Thermogenesis - heat production - while the third
regulates - kept in balance between the two thermogenes.
The thermogenic mechanism is obviously founded
being kept in balance by two opposing influences -
and for inhibitory. The thought that in the
insure - the thermogenic mechanisms must be
larger - one influence outweighing the other
inhibiting the production of heat.
The thermogenic parts consist in the respiratory
respiratory heat - centers in the medulla.
From the evidence before him he thought he
was justified in ascribing little corpuscles a
important part in thermogenesis.
The thermogenic area the leading mechanism
in localization but the experiments - he had account
ofts deemed to indicate Körig's region in the cortex
as the probable situation of it.
Macalister considered that these mechanisms
were developed in order. First appeared the well
organised thomost - thermolytic apparatus - seen
in the lowest in mammals - fishes.
These did cause the thermogenic - yet quite so
fully organized as the thermolytic. It appears
first in the reptiles—which are sometimes cold
sometimes hot-blooded—being particularly well
developed in birds, which are said to have
large corpora striata.

Last appeared the least organized highest
of the three—the thermostatic mechanism—first
in the chick but more fully developed in the adult.
It attributed the difficulty of localising it
to the fact of its being so little organised.

Such a scheme of development is what
would naturally be expected if it be the case, the
relative positions of the preceding mechanisms in the
nervous system would be such as we have already
even hit upon. The thermic has lowest—then the thermo-
genic—lastly the thermostatic.

If we sum up what appears to us so far
as the influence of the nervous system on the
production of heat—we seem to be entitled today
that—at any rate in dogs and rabbits—there are parts
of the brain above the medulla oblongata concerned
with heat-production—that the corpora striata of

(1) W. Bichat states that the corpora striata are smallest
fishes—amphibians—larger in reptiles, much
To a less extent the Optic Thalami leave a special relation to the process probably contain centers which control the chemical changes in the brain.

Also that Hitzig's region of the cortex seems to play a very important part that likewise as the various experiments agree in showing that the function of it leads to increased production of heat. While irritation leads to diminished production of heat, its function is to inhibit chemical activity which the balance between heat production and heat dissipation.

We pass now to the clinical evidence as to the existence of a center or centers concerned with heat production.

And we will see how far the conclusions drawn from experiments on animals are confirmed by observations on man.

Appendix is a list of cases in which there has been disturbance of the temperature after nerve lesions - then being no other reason than discovered for the rise than the nerve lesions.
## Official Corps

<table>
<thead>
<tr>
<th>Rank</th>
<th>Injury Description</th>
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<tbody>
<tr>
<td>1.</td>
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<tr>
<td>12+13</td>
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Note: The table contains handwritten entries which are not completely legible due to the handwriting style.
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<table>
<thead>
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<tbody>
<tr>
<td>15.</td>
<td>[Note:]</td>
<td>Field, 40°E.</td>
</tr>
<tr>
<td>16.</td>
<td>[Note:]</td>
<td>Field, 40°E.</td>
</tr>
<tr>
<td>17.</td>
<td>Navy</td>
<td>100°E.</td>
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<tr>
<td>18.</td>
<td>Age Smith</td>
<td>100°E.</td>
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<tr>
<td>19.</td>
<td></td>
<td>100°E.</td>
</tr>
<tr>
<td>20.</td>
<td>Cape Devolet</td>
<td>60°E.</td>
</tr>
</tbody>
</table>
21. Ridge saga

22. F. Taylor

23. Miles

24. Edmund

25. Alexander

26. John

27. Lepus

28. Henvr

29. Michael

30. Peter

31. 

32. 

Lung montage in Noco

Lung montage in Noco (Odonata 02)


Large cell in R. Lobelia densiflora. Large cell in R. Lobelia densiflora.

Large cell left side of Noco.

Throat in Noco. Throat in Noco.

Almost dead. Almost dead with 30.

High temperature, 108°F. First before death.
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>33. Tolstos</td>
<td>Large house on edge of town where</td>
<td>Actual or actual.</td>
</tr>
<tr>
<td></td>
<td>was offered 1034 assigned.</td>
<td></td>
</tr>
<tr>
<td>34. Ruined</td>
<td>Large old ruin; part of Mars. Reducing</td>
<td></td>
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<tr>
<td></td>
<td>into 30 feet.</td>
<td></td>
</tr>
<tr>
<td>35. Brown</td>
<td>Remonstrate in Pius</td>
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<td></td>
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<tr>
<td>36. Erb.</td>
<td></td>
<td>Pius 1079. 252</td>
</tr>
<tr>
<td>37. Joves</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38. Alexander</td>
<td>Small cell in lower part of town.</td>
<td></td>
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<tr>
<td></td>
<td>Pius 1079. 252. in Pius</td>
<td></td>
</tr>
<tr>
<td>39. Wilde</td>
<td>Remonstrate in Pius</td>
<td>Cardinal Pius 1079. 252. in Pius</td>
</tr>
<tr>
<td>40. Ricker</td>
<td>Remonstrate, Pius 1079. 252. in Pius</td>
<td>Cardinal Pius 1079. 252. in Pius</td>
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<tr>
<td></td>
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<tr>
<td>41. Based on</td>
<td>General offering of Pius is often accompanied by</td>
<td></td>
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<tr>
<td></td>
<td>reductions 1079. 252. in Pius</td>
<td></td>
</tr>
</tbody>
</table>
47. Hemorrhage of brain (cont.)

48. Forensic

49. Dural clamps

50. Section through brain showing area of damage

51. "a"

52. "b"

53. Motor

54. "a"

55. "b"

56. "a"

57. Pia mater

58. "a"

59. "b"

60. "a"

61. 2 cases, considerable damage, plant-like

62. Deflection near fovea of occiput
Other Parts of Brain (cont.)

Necropsy 12th June 1916

70. Head

Blood effused at root of optic nerve. Also in left lateral ventricle. Left lateral ventricle was 1.5 in. in diameter. Extreme dilatation of right lateral ventricle. Also dilatation of third ventricle. The brain was firmly adherent to the dura mater. No tissue could be removed from the cranium. No. 76 continued...
The there are over 70 cases of this instance of leprous cerebrospinal lesion of the sensory type.

At the first sight we are struck with the fact that these lesions are scattered over all parts of the central nervous system, from the cortex to the dorsal part of the cord. But their course as if there were no chance of leaving out any particular area. Only when we come to see them more closely we see that the lesions follow fairly definite lines. With one exception (case 63) to which the rise of temperature was very transient, we may to hold the affected parts from the cortex, i.e. between the central ganglia of the central neuraxis through the pons-medulla oblongata, that is, exactly the part main channels of communication between the central nervous system and various parts of the body.

And such an arrangement is one that we should naturally expect for the parts which have to do with the management of the parts of the body which are in vital connection with the brain. The part which produces lesions, the dorsal region of which lies along these channels from the cord.

In many of the cases related the damage to the brain is so extensive that they are almost useless for purposes of localization. But, on the other hand,
These are to definite circumstances that certain conclusions are strongly denoted. When we come to look into the case with care, we find that there is much evidence to confirm the results indicated by experiment.

Talking first, the 20 cases of lesions of the cord we notice that in nearly all of them it is the cervical part that is affected complicated. From these cases, very little can be gathered for or against the existence of any heat center or centers—because, as all these cases usually play a very important factor—the destruction of apraxia—the significance of which cannot be sufficiently estimated. It is impossible at all in any given instance whether the abolished body heat is due to this absence of the base in the cerebellum, more absent heat being dissipated or whole it is due to the amount of heat produced, and this consideration alone is sufficient to prevent any reliable conclusions being drawn.

It is said that when is the case a wound in which injury of the cord below the level of the first dorsal vertebra has been followed by great lowering of the temperature. And if this be so, it is readily explained by remembering that below that point the abdominal (1) Holmes' System of Surgery I. 654. (1883).
Vascular supply will not be affected - the fibres which go to supply the muscles in the walls of the bloodvessels having left the cord at the level of the intercostal vessels. And descriptio alteration here that could introduce much difference - the condition of the rest of the second party is depending on much on that of the abdominal circulation.

The only thing that can be said is that the center or centres cannot be in the cord, but it is only the fibres that pass from it others that appear there.

In what part of the cord the fibres are, we cannot say. In all the cases but two the cord seems have been injured throughout its whole thickness. But in cases 12 and 13 the anterior columns escaped. In these cases the laceration was considerably subnormal. The might be healed. But for such as Fischer did that a regulating center. Any further that fibres from a beat controlling center pass down the anterior columns if being uninjured left full play for the beat production. The repetition of this account being subnormal.

In case 2 in which the laceration can very high it is asked that the posterior part of the cord especially suffered. But as the whole thickness
allowed to be in truth, we cannot suppose that the anterior columns escaped.

And these considerations are to us the chief speculative until we are able to gauge the effect of the vascular centres.

When we get above the medulla we are on firmer ground for then we are beyond the great heat-dissipating agencies the heat which pervades over the blood vessels of the epidermis.

In nearly all the remaining cases the temperature was elevated. The few exceptions in which there was a fall are all to be explained by the shock of the injury, all the functions being abolished and depressed.

We come upon a number of cases in which the fever the fever a long time after the patient's death. In two cases, one under 21 in the brain affected (in addition to the one of facular abscesses). And indeed as frequently does alteration of temperature follow brain affection, that wood is inclined to think that this is the most probable place for the position of a heat-tolerance centre in man.

Now the fact that the same alterations in temperature follow lesions higher in the brain made us hesitate before we accept this. For we

(1) 1857, p. 185
found in the table, many cases of high temperature accompanying injury of parts in the cortex about the basal ganglia. And these could very well affect such centers as the Pons but also the frontal portions of the brain at a higher level. And when we remember that the Pons is the great channel of communication through which so many of the nerve fibres pass to the spinal cord, it occurs more likely that the result in the temperature which followed injury or disease of the Pons are due to destruction of irritation of fibres which pass through it on their way to the muscles.

Passing next to the remaining cases in which parts of the brain higher than the Pons were affected, we notice that they include 33. And on analyzing these cases, we find that there are at any rate two regions which may be excluded from consideration.

In only 3 instances (cases 43, 48, 53) do the corpora quadrigemina seem to be involved, for all three it is easy to account for the disorder of body heat apart from them.

Thus, in 43, the Pons and the Medulla were injured. In 48, the Pons, Crus cerebri, Optic Thalamus and
Corpora striata have not been observed in necropsy.

While in 144, there was pressureabnormal on the

_Put_Hi Thalami_ but on the Right-Amus cerebri.

In only 4 distances, in the cerebellum involved.

In two cases it was slightly enlarged. Another, 460,

involved also the tons as well as the frontal lobe.

In the part of 45 there was considerable mingling

of fibers passing from the cortex downward.

So that, we may safely consider that the

Corpora striata in the cerebellum having no

thing to do with influencing the cerebrum of the

body.

Passing to other nuclei, at the base of

the brain--the Put_Hi Thalami, the Corpora striata--

we are impressed with the large proportion of cases

in which these ganglia were involved. Only the

33, in no fewer than 17 was the Corpus striatum

directly or indirectly affected. In 15 the Put_Hi

Thalami, amongst these, 7 involved both the

Put_Hi Thalami, the Corpus striatum.

_Corpus striatum._

In 3 cases (47, 59, 67) the Corpus striatum

was the only part of the brain implicated. In 3,

(42, 64, 65), it was the principal lesion. Thus in

case 62, although there were hemorrhage around

...
Dorsal of the cerebral arteries, the softened corpus callosum is the only region that is denuded of any lesion. In case by it was accompanied by injury to the anterior part of the optic thalamus and in 65% of the optic thalamus on one side was also involved. In addition to these, there are 2 cases, 31 and 35, in which it was involved only in the optic thalamus.

Of the remaining 7 cases, 19, had a small spot in the external capsule, the main lesion being the prestriatal involving the under surface of the brain from the ascending pericallosal convolution to the posterior part of the thalamus, thus the optic chiasma was also the official cause.

Another 22 involved the dorsa lenticular, medullary cords.

Another 52, one of the occipital convolutions and the cerebral peduncles. The prestriatal, the centrum ovale. These 69, 66, 71, were large hemorrhages involving several parts. In the 8th case, 56, the affection of the corpus striatum followed multiple cerebral embolias, which were uniformly distributed to other parts.

In the last 50, the hemorrhage was into the centrum ovale the lateral ventricles.

Optic Thalamius.

Of the 18 cases in which the optic thalamus is denuded, in only one, 65, was the only part affected, in that the temperature was subnormal.
In 4 cases, 51, 53, 60, 65 it was with the corpus striatum, the main lesion being in the thalamus.

Of the remaining 15, in 4-53 58, the hemorrhages extended into the thalamus. In one 46, a hematoma prevailed on the crus, inferior peduncle. This was the case of Dr. Martin Ebertsen. In 52, had hemorrhages also in the occipital area via the cerebral peduncle. While in case 57, the bleeding was in the lateral ventricles. The lesion was large.

In these cases 52, 56, 57, 59, the hemorrhaged areas were very large.

The fact that the corpus striatum or thalamus were engaged in a large proportion of cases, makes us wonder, to the belief that, to at any rate, the corpus striatum must have something to do with the production of heat or will to movement.

Especially startling instances are the 4 cases, 47, 53, 60, 65 in which the corpus striatum alone suffered. The other 3, 42, 64, 65 in which it was the principal sufferer.

There is one point difficultly in the way of supposing that there is a heat-producing center in the corpus striatum. That is that which in one case, 47, the lesion is said to have been in the thalamus but outside the tectal nuclear nucleus, in the thalamus 5, 62, 63, 65.
there was considerable destruction of gray matter.
And it is not easy to see how destruction of the gray
matter could cause an increase in its function. It
is possible that the particular area we are supposing
has to do with lead production, as it was divided
by the surrounding part—but such is not a likely
event. Another explanation seems more plausible.
In 3 of the 6 cases, 47, 67, 60, and 67, the black
matter was involved in the destruction. It might be
that the damage consisted in cutting off fibers from a
heat-producing center in the cortex rather than
inhibiting a heat-producing center at the base.
But whatever the explanation may be, there is
much here to explain the experiments of which I
went over the lights of these—though we may not say
definitely that there is a heat-producing center
in the basal ganglia. Yet it is evident that there
is a close relationship between the basal ganglia
and production of heat.

There are 6 of cases of the 33 in which either
the optic thalamus or the corpus striatum was involved.
In one, 43, the tonsillar area was implicated. In another
53, the description of the lesion is not sufficiently defined.
In 7, parts higher in the brain were injured.
Parts higher than the Basal Ganglia.

We will see to what extent the experiments are corroborated by injuries to parts higher in the brain.

In 55 cases the cortex alone was affected, e.g., fracture of the lesser wing of the sphenoid, injuring the front of the lateral lobe of the right hemisphere. The 3rd Right Frontal Convolution. Case 60 was a lesion on the surface of the occipital lobe. In 63, there was the pressure on the tissues of the brain due to the lesion on the posterior part of the temporal convex and the following fracure of the Parietal bone.

In cases 45, 50, 57, 61, 62, the center of the hemisphere was implicated.

Of the other nine cases, 19, 40, 63, in 63, the brain was besides lacerating the lower portion of the descending frontal convolution the Parietal lobe,两人 to the Ethical capsule. The conv. In 52, the hemisnare in the Occipital lobes was less important as the damage in the corneal of the temporal or the frontal bone at the base. In 60, the brain was implicated as well as the Frontal lobe.

In cases 66, 70, 71, the damage was suggestive that the definitive information can be drawn from the lesion. It is well known to state that the localization was in spite of the tendency to the pressure caused by the necessary stretch.
Thus, we have to deal only with the 9 cases, 40, 60, 63, 64, 65, 67, 81 & 62. The common positive evidence is derived from these. But if we accept case 66, evidence may be derived from even the experiments which point to the existence of an area near the thalamus of McCulloch as having to do with that inhibition. And the fact here may be put on the side, for the case in question was too slight in duration to show that it may be tested upon as an accident, due probably to a cause quite apart from the injury to the thalamic area.

At the first sight, case 66, in which there was pressure following depressed fracture of the parietal bone, appears to support the idea that the area in question is near the thalamus of McCulloch— for it is stated that the pressure was on the posterior part of the thalamic area. But it is difficult to imagine that with such a state of things, that part alone would be affected. It seems as though it would be impossible to prevent pressure all over the part where the fracture was, if the neighborhood of the thalamus of McCulloch could so easily escape. All the other cases are injuries near that thalamus of fibres passing from them to the basal ganglia.

Only one, however, is sufficiently well localized.
To convey very definite information that is case 63, in which it is said there was suffering in the neighborhood of the Pons Varolli. Even there, the focal location of the lesion is not accurately given, but if you as it goes, it is the most instructive of all the cases.

The Clinical evidence then bears out very well the indications given by the many experiments. I have learned from it that in all the cases of high temperature enucleated, the lesion has been somewhere along the line from the cortex near the Pons Varolli (near near the Pons Varolli in the area there is 125 sheets) down through the Corona radiata to the Pyriform, the Thalamus, the Corona strata - by the capsule cerebri, the Nuc, the medulla. Also, that the corona striata seems to be especially concerned with the function of heat production, though it is impossible today whether there is a center in that position or if there it is simply on the line from a center in the cortex.

Also, that if there be a center that has to do with the heat of the body at all (as seems most likely), there must be one in the cortex. That it is
inhibitory in character, we cannot claim
that anything more definite than this
has yet been proved.

Such then is the limit of our
knowledge if we would summarize our
present knowledge of the condition of fever.

We should say that there can be no doubt that
the essence of the process consists in increased pro-
duction of heat, which arises from increased
muscular activity.

Also, that it is probable that sometimes this
increased muscular activity is brought about by
changes in the blood or in the general perfusion
of the body.

That certainly it is produced directly by
changes in the nervous system. Some part or
part being acted on by the form-producing cause.

Then we come to examine the nervous
mechanism concerned, and we are certain only
of one part of it. Namely, that there are centres
which produce over the loss of heat—the vasom-
ulatory, respiratory, sweat-centres in the medulla
ossal.
But there is strong evidence that the corpus striatum (perhaps the whole thalamus) has an intimate relation of some kind with the production of heat. That there is an area in the cortex, most likely near the fissure of Rolando, which seems to have for its function the inhibition of heat-production.

[Signature]

Edward Waller