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The nature of fever in re-  
-lation to certain methods of  
treatment

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It is difficult and even im-  
-possible to draw a sharp  
distinction between the specific  
fevers so-called and those inflam-  
-mations which are attended  
by general constitutional disturbance.  
A few diseases which are generally  
regarded as pure inflammations  
such as Pneumonia are thought  
by some to depend on a specific  
poison and many specific fevers  
are attended by local inflammations  
which form an important  
factor in their history. In speaking  
therefore of fever in general  
terms acute inflammations are  
necessarily included.

The nature of fever has of course  
been much discussed in all ages



and even at an early period some glimmering of the truth seems to have been perceived; but until very recently men  
 This has been hidden in a cloud of erroneous ideas arising from ignorance of physiological processes. Even now it is necessary in considering the nature of fever to keep the point under discussion clearly in view and not to con-  
 -found it with closely allied subjects.

The chief stumbling block in the way of a correct knowledge is the confusion which arises from jumbling up together the cause, the nature, and the effects of fever.

These three things are different from each other and in all discussions must be kept rigidly apart.

The cause of fever may be a poison introduced into the blood, or

or a local inflammation  
 This poison or inflammation by  
 its action on the blood induces  
 changes in the tissues of the  
 body, and these changes constitute  
 the intimate processes of fever  
 and give rise to its essential  
 phenomena. These changes also  
 produce results in various organs  
 which must be distinguished as  
 the effects of fever and not having  
 any necessary connection with its  
 nature.

Suppose a poison to have entered  
 the blood it seems probable that  
 its action is two fold (1) It reproduces  
 itself and (2) it induces some kind  
 of change in the blood.

It must be assumed that this  
 blood change occurs:

(1) Because in most fevers  
 a period of incubation occurs.  
 If the poison were itself able  
 to excite fever why should it  
 not do so at once?

(2) The fever generally leaves the organism protected, for a period at any rate against a second attack. It is reasonable that some blood change confers this immunity. Modern theories and experiments render it probable that some low kind of fungus is the cause of several fevers. It is known that such fungi readily excite a change, to wit a fermentation in any fluid into which they may be introduced. It seems therefore that a change like fermentation results from the introduction of the fever poison into the blood and that the products of this process acting on the tissues induce the phenomena of fever. Up to this point nothing of the true nature of fever has appeared; the process indicated is merely the operation of the cause. A profound blood change has doubtless been induced

a change potent for evil to the existence of the organism; but if the process stopped here if it went no further than this blood poisoning, no phenomena of fever would appear, death might occur, but it would not be death from fever. In fact the products of this fermentation in the blood themselves constitute, by their action on the tissues, the immediate exciting cause of fever.

If this be true it follows that all methods of treatment which aim either at preventing the entrance of the original poison into the blood or at its destruction in the blood are preventive methods of treatment and it seems to me that specifics such as Salicine in Rheumatism and Quinine in Ague ought to be regarded as preventive remedies.

The action of the products of fermentation upon the tissues results

in the familiar phenomena of fever, of which the most striking and important is the rise of bodily temperature. There can be no doubt that in the method of production of this rise of temperature the whole mystery of the fever process is involved.

The first question which has arisen at this point is whether the rise of temperature is due to successive production of heat within or diminished loss of heat from the body.

This question may now be considered as settled; there seems no room to doubt that loss of heat in fever is not only not diminished, but is even increased.

It has been proved that a body suffering from fever will warm a given quantity of water more rapidly than when its temperature is normal. Radiation must be more rapid from a body at a high temperature than at a low one, and the increased

frequency of respiration provides for greater loss of heat by the lungs. If there be no diminution in loss of heat there must necessarily be increase in its production, and evidence that this occurs is at hand in the increased quantity of products of oxidation, of which the types are urea & carbonic acid, secreted during fever.

This heat can only be supplied in the body, under the circumstances of fever in one way, that is by chemical action; and physiologists have shown pretty clearly that such chemical action occurs only in the protoplasm of the tissues. The blood serves no other purpose in health than to carry oxygen and nutritive substances to the tissues and effete matter from them; it has been degraded from its former position as the grand scene of the oxidation of the body; in fever it carries

8

the poison to the tissues upon which it acts, but it takes no further part in the processes of the disease, these go on wholly in the protoplasm of the tissue, the fever does not rage in the blood.

This increased chemical action in the tissues, or metabolism, is then one fundamental point in the nature of fever, and is the immediate cause of the rise of temperature which is pathognomic of this condition. There remains however another point of vital importance to be considered.

In health the most striking fact among the phenomena of animal heat is that great balance which is maintained between production and loss of heat so that a nearly constant temperature is maintained.

The consideration of this equilibrium affords abundant <sup>evidence</sup> of the control

directed by the nervous system over  
 the phenomena of animal heat,  
 and it appears that its maintenance  
 is a primary object of that control.  
 By means of an <sup>and</sup> such active vaso-  
 -motor mechanism the quantity of  
 blood in any given area of  
 the body is readily controlled and  
 altered; if heat be produced too  
 rapidly the blood supply to the  
 surface is increased and a more  
 rapid cooling counteracts the effects  
 of increased production by increased  
 loss and vice versa.

In fever this normal equilibrium  
 is disturbed; the loss does not  
 balance the production and the  
 temperature rises. But it does not  
 continue to rise indefinitely, sooner  
 or later a new equilibrium  
 is obtained and the temperature  
 remains at or about a new  
 "pathological normal" if such  
 an suppression may be allowed.  
 This shows that the control of

The nervous system of an animal that is disturbed and fevered in fever, but it must not be supposed that it is lost.

In some cases indeed (hyperpyrexia) this seems to occur; the temperature continues to rise to a great height. There is evidence of profound affection of the nervous system and death occurs. Here production of heat seems to have run riot in the body without any controlling influence of the nervous system and we may suppose that in such cases its influence has been destroyed.

It appears then that there are two great factors in the essential processes of fever, namely increased tissue metamorphosis resulting in increased production of heat, and a perversion of the normal controlling influence of the nervous system over the phenomena of animal heat.

The question next arises are these two factors independent of each other, or is one secondary to the other and if one which?

I think that at present no attempt can be made to answer this question. If the matter be clearly laid down for consideration probabilities seem to be pretty much as follows. 1<sup>st</sup> It seems reasonable to suppose that the action of the fever poison on different kinds of tissue may be attended by different results. On the general tissues of the body especially the muscles and great glands, a part of whose most important functions is the regular production of heat by their metabolism it is easy to suppose that the action of such a poison would itself stimulate that metabolism & give rise to increased heat production. At the same time the poison

12

acting on a peculiarly constituted tissue such as the nervous, which plays but a subordinate part in the general business of heat production, would produce peculiar effects, of which one might be a perverted control over heat phenomena, as a perverted influence over the circulation might be another.

Thus these two factors might fairly be regarded as independent effects of the same cause acting on different tissues.

2<sup>nd</sup> It is certain that the nervous system exerts a powerful influence over all the functions of the body; the manifestation of this influence may be often puzzling and mysterious but its existence cannot well be doubted. This being so it would not be irrational to suppose that the poison acting on the central nervous organs so perverts

19  
their influence, that the increased tissue metamorphosis and other manifestations of fever are merely secondary phenomena dependent on a functional nervous disorder.

In the same way a contrary theory might consider the nervous phenomena of fever to be secondary to the increased metabolism of nerve tissue.

These considerations seem at present to mark the boundaries of our knowledge of the nature of fever; but the phenomena discussed produce effects which although they must be considered secondary in relation to the essential processes of fever, yet practically and for clinical purposes possess an overwhelming importance.

Of these effects I think three stand out above all others in their influence over the course of the disease and as rational effects for effective treatment. These are

- 14
- (1) disturbance of the circulation
  - (2) accumulation in the blood of waste products of metabolism,
  - and (3) defective performance of the functions of digestion and assimilation.

The disturbance of the circulation seems generally to take the following course: First a period of increased arterial blood pressure, with tense pulse and regular forcible action of the heart, gradually giving way to relaxed arterioles, low blood pressure and rapid feeble and even irregular action of the heart.

This condition requires examination: The high blood pressure of the early stage may be attributed to one of two courses; either it is produced by a poison in the blood acting locally on the protoplasm of the arterial muscular fibre cells & causing their contraction; or it is due to the interference of the central

nervous organs through the vaso-  
-mota nervis.

The experience of kidney disease teaches us that the circulation of certain poisonous substances in the blood, namely, products of tissue metabolism, acts powerfully in constricting the arterioles and thus raising the blood pressure without any interference of the central nervous system.

We might at once conclude that in fever there is a perfectly analogous case, here also products of tissue metamorphosis are circulating in veins, and we may suppose that they act on the arterioles just as in kidney disease.

But this analogy can hardly be maintained.

The rise of blood pressure in fever occurs only at the commencement of the attack before one could expect to find much of these substances in the blood, and at a

16

latent period when they are in-  
-doubtedly <sup>present</sup> in <sup>success</sup>, the blood  
pressure is abnormally and even  
dangerously low.

There appears to be no evidence  
of any special action of the fever  
poison upon the arterioles or  
upon any local nervous me-  
-chanism in connection with  
them; neither is there any direct  
evidence of interference of the central  
nervous organs.

But it must be remembered that  
the nervous system gives evidence  
of great & far-reaching perversion  
of function at the commencement  
of fever. The rigors, vomiting  
and in children even convulsions  
which constantly usher in these  
attacks must surely be attributed  
to nervous action.

Further the rise of blood pres-  
-sure has in most kinds of  
fever only a very short duration,  
it does not seem to depend on

17  
any abiding cause, and in this way has some resemblance to the rigors and other nervous phenomena.

If the rise of blood pressure depend on the presence of a poison in the blood we might expect it to continue as long as the poison is there, but it has in most cases only a short duration, which itself may be regarded as evidence of nervous interference.

Whatever be the cause of this rise of blood pressure I think some cases occur in which its presence & persistence constitutes a grave danger to life.

Sometimes, notably in the so-called sthenic forms of Pneumonia & in fevers which accompany acute brain affections this rise of blood pressure seems to be anything but a transitory affair. In such cases we see a fierce struggle for supremacy between

the heart on one side and the muscular fibres of the arterioles on the other, the latter by their persistent contraction obstructs the passage of the blood into the veins, the arteries become overfull and an extra strain is thrown on the heart, which redoubles its exertions in order to overcome the obstruction.

Thus the two antagonists react on one another until both are exhausted by the conflict; the arterioles give way and a condition of low blood pressure remains.

The whole arterial system with the heart is left in a state of exhaustion and ill-calculated for the proper performance of its functions during a period extremely critical for the organism. A period of low blood pressure always follows the initial rise and may be considered the normal

19  
Condition during the greater part  
of the course of fever.

If it become successively low  
& constitutes a danger, and nothing  
is likely to cause an excessive  
fall as an excessive rise at  
the early stage. Thus the condition  
of the circulation though it must  
be regarded as a secondary matter  
among the essential phenomena  
of fever becomes by its influence  
on the course & result of the  
disease a subject of the first  
importance.

Of the presence & accumulation  
of white matter in the blood  
and the importance of facilitating  
their removal; of the disorders  
of digestion & assimilation, it is  
not my intention to speak.  
They are to be borne in mind  
& referred to incidentally. They  
are important subjects but  
have little direct <sup>bearing</sup> on my  
present purpose.

By the light of the above remarks it is my intention to discuss the value of two methods of treatment which I will call the antiphlogistic and the antipyretic. The antiphlogistic method after having been for a great length of time the almost universal method of treatment for acute diseases, has been deposed from its high position and is now treated with almost universal neglect.

This neglect is I think largely deserved; but it may be useful to consider under what circumstances benefit might be expected from the employment of antiphlogistic measures in fever.

The most important antiphlogistic measure and that around which the whole question of this method has centered is of course blood-letting. Few will dispute the value of local blood-letting by leeches & so on in the early

stages of various inflammations,  
 the way in which it acts is  
 not easily explained, but the  
 benefit in many cases is so  
 marked as to be indisputable.  
 The benefit however to be derived  
 from general blood-letting is  
 a much more problematical  
 affair. It is justly regarded as  
 a formidable remedy. Many theories  
 of its action have been evolved  
 of unsoundness, and physiologists  
 having found that in the healthy  
 individual it produces little  
 effect on the circulation unless  
 carried to a dangerous point;  
 many have concluded that it  
 can under no circumstances  
 be beneficial, & have rejected  
 it entirely.

It is absurd to suppose that  
 by the abstraction of blood the  
 febrile process can be cut-  
 short or its severity mitigated  
 by removal from the body

of a portion of its poison, or that its violence will necessarily be checked by resort to lowering measures. It seems that the putrid process itself is far removed from reach of such measure as bleeding; if this remedy can have any effect on the course of an attack of fever that effect must be looked for among the secondary phenomena or results of the process. Bleeding if it affects anything in the body affects the circulation, and if it affects any of the phenomena of fever it affects the circulatory phenomena. If it act in any way upon the circulation it must be by lowering blood pressure, and if there be any danger in fever from too high blood pressure we might expect to counteract this danger by blood-letting. It has

been said that the blood pressure is raised in the early stage of fever, & I believe that this is always so though in the case of the continued fevers the condition is very transitory. In others such as the fevers which accompany inflammations like Pneumonia or Peritonitis it is often persistent & constitutes a danger. I now attempt to show that a persistently high blood pressure with abnormal distension of the arterial system must necessarily produce exhaustion of the muscular fibres of the heart and small arteries. When this exhaustion reaches a certain point - these fibres give away, their efficient contraction being no longer possible, a period of low blood pressure follows, which may be supposed to be more marked in proportion as the previous overstrain of the arterial system has

been excessive.

A state of abnormally low blood pressure, with great exhaustion of heart and arteries during the later stages of fever, when all the organs & functions of the body are enfeebled, seems to be a condition to be avoided if possible, being fraught with danger to life. Hence I think we might hope that an early blood-letting by checking or controlling the excessive rise of blood pressure would prevent the subsequent dangerous state of exhaustion and in this way prove the means of saving life. Cases of the kind I have mentioned are no doubt rare but I am convinced they do occur & I have seen some cases of Pneumonia fatal at an early period, in which a very hard moderately quick pulse with forcible heart's action, giving way to one exceedingly feeble & irregular seemed to favor this view.

Physiology objects that bleeding within moderate limits has no lasting influence on blood pressure in the healthy body. To this it may be answered that the processes of health are carried on and its maintenance secured by a vast system of compensations; and any obvious change at one point is rapidly & effectually compensated by the whole energy of the economy. In disease this system of compensations is disturbed, & the high blood pressure of early fever is itself a result of this disturbance. Under these circumstances it is reasonable to expect that a measure which can influence only slightly, when compensation is perfect, a normal blood pressure might be expected in lowering an abnormally high one when it is so to speak thrown out of gear.

Shan will not permit a discussion of the action of other antiphlogistic measures such as vomiting, & purging, their action though less powerful is further reaching and of wider application than that of bleeding, and hence their use is more readily admitted. It must not be forgotten however that one of their results is a lowering of general blood pressure.

They relax the walls of the abdominal vessels into which a great quantity of blood can be collected & from this blood they abstract a quantity of watery fluid. Such an action may be expected to exert a considerable influence over general blood pressure.

It may then be concluded that owing to the very short duration of the high pressure period and to the lowering nature of the fibrile process the employment of the grand antiphlogistic measure of

bleeding is as a rule inadmissible but that in certain cases of Pneumonia Peritonitis and other inflammatory disorders it offers a fair prospect of benefit.

But if it be done at all it must be done early in the attack and not left as it usually is until every other remedy has failed and the patient is obviously beyond the reach of ordinary measures. To perform phlebotomy then, is to my mind only to hasten the inevitable end, by employing a remedy at a time when the circumstances under which it might be beneficial have long passed away.

I turn from a method whose days have gone, to one which is at the present moment and its trial, the antipyretic method.

Since the invention of thermometry the study of temperature in fever has been a constantly increasing

Delight to men's minds until  
 some have almost begun to  
 reverence the temperature of fever  
 as the disease itself. Its true  
 importance seems to me to be  
 clear; it is a most subtle &  
 delicate indicator of the progress  
 of the case & according to its  
 rise or fall the patient will  
 generally be worse or better;  
 but its rise & fall is an effect  
 and not by any means a cause of  
 the unfavorable or favorable progress  
 of the case. The temperature though  
 demanding the most careful study  
 & consideration & even to be looked  
 as an oracle in gauging the  
 effects of any therapeutic agent,  
 does not necessarily require  
 treatment. To our predecessors  
 the pulse was the grand indicator  
 of the progress in fever & accordingly  
 they set to work to treat it  
 with vigorous antiphlogistic measures  
 which becoming abused led to disaster

and violent revolution.

May not some of us by treating our great indicata be running into similar danger?

Antipyretic remedies <sup>are</sup> ~~may be~~ of two kinds, external application of cold and internal employment of certain drugs; their mode of action is different and they must be separately considered.

Internal application of cold can reduce temperature in fever only by increasing the loss of heat from the body. If it have any influence over heat production it must increase that also by driving blood into the deep tissues where its presence will favor rapid oxidation & production of heat. Now if the principles formerly laid down be true, no process which while it ~~will~~ may effectually secure rapid heat loss, leaves production unaffected can be regarded as of much

value as an antagonist to  
 the actual progress of fever.  
 It does not strike at the  
 citadel itself, can it be  
 made effectual against any  
 of the outworks? - I think perhaps  
 it may be beneficial in two  
 ways. 1<sup>st</sup> The application of  
 cold to the skin for short  
 periods of time at considerable in-  
 tervals seems to have an influence  
 over the circulation. After the  
 initial rise the blood pressure  
 throughout the rest of the attack  
 is low, the arterioles relaxed &  
 the heart acting feebly.  
 This is probably largely due to  
 exhaustion of the vaso-motor  
 nerve mechanism.

The application of cold to the  
 skin appears to counteract this  
 exhaustion, the vaso-motor nerves  
 are stimulated to fresh action,  
 the pulse becomes firmer & the  
 heart action stronger. By these

who supply external cold in the routine treatment of moderate cases of fever this improvement of the circulation is pretty generally insisted upon; I think it is reasonable to admit that the measure has this beneficial effect.

That this amount of benefit is sufficient to warrant the use of the cold bath in every case of day typhoid fever when the temperature rises above  $102.2^{\circ}$ .

I deny  
 2<sup>nd</sup> The question arises may the temperature itself though usually to be regarded as a friendly indicator of the progress of the case in some exceptional cases become itself a source of evil & it is possible that simple hotness of the body apart from any other cause can impair the functions of its various organs I think it is possible and that

It sometimes actually does so. The advocates of cold bathing have given us glowing accounts of delirious patients, who refused food & appeared to digest it badly, after the bath & with their temperatures lowered reading the newspaper calmly & taking readily food which seemed to agree with them.

Patients with high temperature ( $104^{\circ}F$  to  $105^{\circ}F$ .) have shown some improvement in other respects, after the simple reduction of temperature, delirium has been checked, food taken with less difficulty & so on.

When we recollect the extreme delicacy of the various organs, especially the brain it requires no stretch of imagination to suppose that raising their temperature unduly might disturb the performance of their functions & disturbance of function in the

first instance gives rise to  
 excessive heat production &  
 elevation of temperature; this  
 elevation of temperature may  
 I think if excessive, be supposed  
 to react again on the organs  
 & produce further disturbance of  
 function. We know at any  
 rate that elevation of temperature  
 favors that chemical action which  
 is itself the source of heat  
 The cold bath may thus be  
 of use in two ways & I think  
 it can be used with benefit  
 in cases of fever with very  
 high temperature, when there is  
 besides much disturbance of the  
 functions of the various organs  
 In cases of threatened hyperpyrexia  
 I should invariably employ it  
 as the only remedy which can  
 give the patient a chance of  
 escape from what otherwise appears  
 to be inevitable death. The dogged  
 pertinacity with which the temperature

goes on rising in these cases  
 and the helpless delirious  
 condition into which the patient  
 rapidly sinks, presents a really  
 appalling spectacle, & justifies  
 the employment of any measure  
 that offers even a chance of  
 success. The futility of any  
 internal remedies at present  
 known is beyond question.

Of Antipyretic drugs, neither  
 the mode of action nor the  
 efficiency is clear. Quinine,  
 Salicine, Kainin & Antipyrin  
 have all been credited with  
 the power of reducing temperature  
 & have been used with that  
 purpose in fever.

The first questions regarding  
 them are: Do they increase heat  
 loss or diminish production, or  
 do they act through the nervous  
 system, & thus reduce the  
 "pathological normal" temperature  
 to a lower level?

I do not think that either of these two questions can at present be answered with any show of evidence. Two things however seem to be true of these drugs 1<sup>st</sup> Their advocates only claim for them that they control the temperature & thus eliminate any evil results directly arising from that cause; they do not cut short the disease itself

2<sup>nd</sup> All except Sevin are powerful depressants. The one at present most in use is Antipyrin and this is so depressing that it requires a stimulant to be given with it to counteract its depressing effect. The action constitutes a grave objection to the use of these drugs which is not counterbalanced by any evidence which I have yet heard in their favor. They are however on their trial & it is necessary to

to wait for further evidence  
before attempting to decide what  
their mode of action is or  
to measure their therapeutic  
value.

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