CHAPTER XVI.

THE MODE OF ACTION OF THE SALICYL COMPOUNDS IN RHEUMATISM.

BETWEEN rheumatic and intermittent fevers there exist not only pathological but therapeutic analogies. The pathological analogies have already been dealt with. The therapeutic have now to engage our attention.

It is scarcely possible to study the therapeutic effects of the salicyl compounds in acute rheumatism, without comparing them with those of quinine in ague. The analogy forces itself on our notice.

Either remedy manifests its effects by a prompt alleviation of all the symptoms of the disease; to ensure its full beneficial action, each has to be given in large and frequently repeated dose, and for some time after the acute symptoms have disappeared; and neither produces the same marked effects in any other ailment.

Holding, as we do, that the poisons of rheumatism and of ague, though specifically distinct, are similar in nature and in mode of action; and finding that the morbid process to which each gives rise may be arrested by large doses of somewhat similar remedies, we cannot but regard it as at least probable that the mode of action of the remedy is the same in both—that the salicyl compounds cure rheumatic fever in the same way that the cinchona compounds cure intermittent.

How each exercises its curative effect is the question which we have now to consider.

Let us first take the cinchona compounds.

That the cinchona alkaloids arrest the course of intermittent fever is an established fact in practical therapeutics. How they do so has never been explained. "Ague is the disease of all others in which the power of medicine, both as regards prophylaxis and treatment, is most marked. We know that if a man pass through certain districts, and more especially if he sleep in them, he is likely to be attacked with a fit of shivering which, after lasting some time, will be succeeded by a

burning fever, and then by profuse sweating, after which he will feel comparatively well until the next day, when another shivering fit will come on at the same hour and run the same course as the first. We know that by warning the man against the dangerous locality, or by making him adopt certain precautions, take cinchona alkaloids, if he cannot avoid the place, we may be able to prevent the disease; by administering one large dose of quinine before a paroxysm we may stop its approach, and by continuing the remedy we may prevent its recurrence altogether. But we have no notion of the manner in which quinine counteracts the malarial effects."

There are two ways in which the curative effects of quinine in ague may be produced: either the quinine may so act on the system as to render it insusceptible to the action of the ague poison; or it may so act on that poison as to deprive it of its power of affecting the system. In other words, the action of quinine is either on the system, or on the poison. Let us inquire which it is. And first, let us take its action on the system.

Quinine in large dose (10 to 30 grains) possesses in a remarkable manner the power of lowering the temperature of the body, when unduly elevated. How it exercises this power is not known.

It has been supposed to be due to a special action of the quinine on the nervous centres; and if we recognize the existence of a special thermic centre, regulating the production and distribution of heat, as the vaso-moto centre regulates the distribution of the blood—a supposition in favor of which much may be said—this explanation might be regarded as a very feasible one.

Binz thinks this effect of quinine is to be explained by its lessening the ozonizing power of the blood, and so checking oxidation. All that we really know, and all that concerns us at present, is that quinine in large dose lowers febrile temperature. What we have to consider is whether or not its curative effect in intermittent fever is due to this property, or to some other and special remedial action.

In virtue of its febrifuge properties, quinine has been administered in all febrile ailments. It was at one time claimed for it that it pos-

[1] Pharmacology and Therapeutics, by T. Lauder Brunton, M.D., F.R.S. 1880.

sessed the power of cutting short typhus. More recently it has been claimed for it, as for other febrifuge remedies (the cold bath and salicylic acid), that it exercises a distinctly curative action in typhoid fever, and shortens the duration of that malady. But this conclusion is not supported by the evidence. There is no proof that quinine either shortens the duration, or lessens the dangers, of either typhus or typhoid fever; or that it exercises a distinctly curative and curtailing effect in any other form of fever than intermittent and remittent.

The point is one which could be readily proved, and would long ago have been proved had the facts been as some have stated them to be.

I have frequently given quinine in large dose in all febrile ailments. My experience entirely coincides with that of Murchison, who says, with reference to both typhus and typhoid fevers, that he had "seen no evidence that, at whatever stage it was given, it shortened the course of the disease or diminished its danger."[1]

With the exception of the external application of cold, quinine, given in large dose, is the most powerful febrifuge remedy we possess. There is probably no febrile ailment in which it might not pull the temperature down. But in every such ailment, except intermittent and remittent fevers, this depression is temporary. While the temperature is lowered by quinine, the morbid process which constitutes the disease still goes on; by-and-by the antipyretic effect of the drug passes off, and the disease runs its course, uninfluenced by what has taken place.

So it is with all the continued and communicable fevers. Quinine has no power to arrest their course. Where there is trouble or danger from mere elevation of temperature, it may do good by lowering this. But there its usefulness ceases.

In intermittent fever the case is very different. Here the quinine actually cures. It puts a stop to the whole morbid process, and all that constitutes the disease; and it does this so constantly, so speedily, and so certainly, and its beneficial effects are so lasting, that one cannot fail to see that they are altogether peculiar, and altogether different from those got from its administration in other febrile ailments.

That the action of quinine in arresting the course of intermittent fever is not to be explained solely by its febrifuge properties, is further

[1] Murchison, op. cit.

shown by its power of preventing such fever. Given during the intermission, it prevents the fever from coming on. It exercises a distinctly prophylactic action. Taken regularly by those living in malarial districts, it prevents them from suffering from the action of the poison of intermittent fever. It exercises no such action in any other febrile ailment.

Besides its febrifuge property, quinine possesses no other special action on the body by which its curative effect in ague can be explained. This property does not account for its remarkable power of arresting the progress, and guarding against the occurrence, of that disease. We are thus forced to the conclusion that the curative effect of quinine in intermittent fever, is not to be explained by any action which that drug exercises on the system.

The only alternative view is that it acts on the poison of intermittent fever, and deprives it of its power of affecting the system.

There are two ways in which quinine might deprive the ague poison of its morbific action. It might supply to the poison the second factor requisite to its propagation, and so prevent it taking this from the system; or it might simply destroy the poison.

The first is extremely unlikely. Indeed it is difficult to find anything to say in support of it, except that it is possible. It is not at all certain that such an action might not be accompanied by considerable disturbance. But even if it were not, it could scarcely result in a cure of the disease. It would simply lead to the continued development of the ague poison during the whole period of the administration of the quinine, and to an outbreak of the disease when the drug was stopped. For the large quantity of poison which, on this view, would necessarily exist in the system at that time, would find there the material necessary to its growth and propagation, and consequent morbific action, just as it would have done had quinine never been given.

The view that quinine acts by destroying the malarial poison, has much more to commend it.

Regarding this poison, as we do, as a minute organism, there is nothing improbable in the view that quinine should exercise a destructive action on it; for we know, from the investigations of Binz, that quinine possesses in a remarkable manner the power of destroying many minute organisms.

It thus consists, both with what we believe regarding the ague poison, and with what we know regarding the action of quinine, that the latter should have the power of destroying the former.

It is scarcely necessary to point out that the possession of this power would quite explain both the prophylactic and curative actions of quinine in intermittent and remittent fever.

That such is really the mode in which quinine acts in these maladies, seems to me in the highest degree probable.

We were led to consider this mode of action by the failure of the only alternative mode, viz., its action on the system, to explain the curative effects of the drug. We are led to adopt it by finding, not only that it explains that action, but that this explanation consists with all that we believe regarding the nature of the ague poison, and all that we know regarding the action of quinine on minute organisms, such as we believe the ague poison to be.

But, it may be said, if quinine owes its curative effects in intermittent and remittent fevers to its power of destroying minute organisms, why is it only in these maladies that this curative power is manifested? There are many other ailments which are believed to be produced in the same way, but in not one of them does quinine have the same power of arresting the morbid process.

In the natural history of minute organisms there is no fact better established than that such organisms are possessed of specific differences of whose existence their external form gives no evidence. Two organisms may be indistinguishable from each other by the highest powers of the microscope—so far as can be made out by such examination, they are identical. But it may be found that the one flourishes under conditions which are fatal to the other. In the case of parasitic organisms, this is specially observed; each has its own habitat, in which alone it flourishes, and in which other organisms die.

Again, an agency which destroys one organism may have no effect on another; though the two may be apparently identical. A remedy, therefore, which cures one disease by destroying the organism which gives rise to it, does not necessarily cure all diseases owning a similar causation. Hence quinine may cure intermittent and remittent fevers by destroying the organism which produces them, without having a

like destructive effect on the organisms which give rise to diphtheria, small-pox, scarlatina, typhoid fever, etc.

Poisons possessed of specific differences may have these differences manifested, not only by the different effects which they produce on the system, but by the different effects which other agencies have on them.

The fact that quinine does not shorten the duration of all diseases caused by the propagation of minute organisms in the system, is no proof that it does not owe its power to cut short intermittent fever, to a destructive action on the organism which gives rise to that malady. The fact that it does cut short this fever, is to be accepted as a hopeful indication that other remedies may be found capable of exercising a similarly beneficial effect on other forms of fever whose course we are now powerless to control.

It is, indeed, in the recognition of this view—that the curative effect of a drug may be due to its action on the poison of the disease, rather than on the system in which it occurs—that lies the main hope for the future discovery of remedial agencies, calculated to arrest the course of maladies which owe their causation to the propagation of minute organisms in the system. The discovery of the anti-rheumatic action of salicin was the result of no hap-hazard experiment; but a legitimate inference drawn from the views which I held, first, regarding the nature and mode of production of rheumatism; and second, regarding the mode of action of quinine in those diseases to which rheumatism is most nearly allied.

It was the belief (1) that the rheumatic poison was allied in nature to that of intermittent fever; (2) that both were minute organisms; (3) that the morbific effects of each were due to its propagation in the system; (4) that the curative effects of the cinchona compounds in intermittent fever, were attributable to their destructive action on the poison of that disease;—it was this belief that led me to the conclusion that salicin was not unlikely to exercise a like destructive action on the poison of rheumatism. If quinine destroyed the poison of intermittent fever, it seemed to me, for reasons already given, that salicin was not unlikely to exercise a like destructive action on that of rheumatism, and a like curative effect on the disease to which it gave rise. That it does produce this curative effect has been abundantly demonstrated. The

success of the practice is an argument in favor of the pathological and therapeutic views on which it was founded.

All that has been said regarding the action of the cinchona compounds in ague is, *mutatis mutandis*, applicable to the action of the salicyl compounds in rheumatism.

The analogies which are believed to exist between the poisons of intermittent and of rheumatic fever, have already been pointed out. We regard each as a miasmatic organism which is reproduced in the system, which owes its action to such reproduction, and which is destroyed during the course of the disturbance to which it gives rise.

Between the cinchona compounds and the salicyl compounds there are also marked analogies.

1. The most prominent of these, is the power which each possesses of curing a miasmatic fever. The cinchona compounds cure intermittent, the salicyl compounds cure rheumatic fever.

2. The cinchona compounds are possessed of no physiological action by which their power to arrest the course of intermittent fever can be explained.

It is the same with the salicyl compounds. On the non-febrile body they have no action by which their curative effects in rheumatic fever can be accounted for.

3. It was at one time hoped, and has been at various times asserted, that quinine would arrest the course of other fevers than intermittent and remittent. But though it has been established that quinine in large dose lowers the febrile temperature, often several degrees, it has been equally established that this effect is only temporary, and that the only fevers in which it exercises a distinctly curative action, are intermittent and remittent.

It is the same with the salicyl compounds. It has been hoped, and over and over again asserted, that they possess a curative action in the same febrile ailments over whose course quinine was at one time believed to exercise a controlling influence. But the result has been the same as with the cinchona compounds. Though the salicyl compounds have been proved to be possessed of febrifuge properties, they exercise no distinctly curative effect in any febrile ailment except acute rheumatism.

As febrifuges they are much inferior to quinine. I have frequently

seen a couple of ten-grain doses of quinine, given the one an hour after the other, lower the temperature three or four degrees, after several hourly thirty-grain doses of salicylate of soda had failed to have any effect.

But though the salicyl compounds possess the febrifuge property to a less extent than the cinchona compounds, they are not devoid of it. Salicylic acid especially possesses this property very distinctly. And we have now to inquire whether or not their beneficial action in acute rheumatism is due to this, or to some other special curative effect.

It is with the salicyl compounds in rheumatism as with the cinchona compounds in ague—there are but two ways in which their remedial action can be explained. Either they so act on the system as to render it insusceptible to the action of the rheumatic poison; or they so act on the rheumatic poison as to render it incapable of acting on the system. One of these it must be; for there is no other possible.

First, as to their action on the system.

Like quinine, the salicyl compounds have no effect on the temperature of the non-febrile body; but possess, in an undoubted manner, the power of lowering that of the febrile body. Salicylic acid possesses this property to a much greater extent than salicin.

To produce its antipyretic effect, salicylic acid requires to be given in much larger dose than quinine; and even then its action is less certain and less decided than that of the cinchona alkaloid.

In virtue of its febrifuge properties, it has been administered in nearly all febrile ailments, with varying results. Riess has maintained that it shortens the duration of typhoid fever. I have given it freely in both typhus and typhoid fevers, and never found any evidence that it either shortened the duration, or diminished the mortality, of either of these maladies. This seems to be the experience of most observers.

Were Riess right on this point, the accuracy of his statement would have been placed beyond doubt before now; for salicylic acid was freely used in typhoid fever before it was given in acute rheumatism. Its remedial power in the latter was matter of demonstration five years ago, and is every year made more certain. Its remedial power in the former has never been demonstrated; and evidence is every day accumulating to show that Riess erred in attributing such an action to it. On

several occasions it has seemed to me to exercise a depressing and injurious action.

Evidence all tends to show that it is with the salicyl compounds, as with the cinchona compounds—they are possessed of undoubted febrifuge properties, but there is but one febrile ailment in which they are known to exercise a distinctly curative effect. In other fevers they may for a time lower the temperature, but they do not materially alter the course, or curtail the duration, of the malady. In rheumatic fever alone they put a stop to all that constitutes the ailment—the local inflammation and pain, as well as the general febrile disturbance.

Acute rheumatism does not consist solely of fever. An essential part of its existence is inflammation of the fibrous textures of the motor apparatus.

Just as it is impossible for any poison to produce the disease without causing inflammation of these textures—so it is impossible for any remedy to cure it, without allaying that inflammation.

The fever and the local inflammation are essential parts of the disease. Fever does not cause inflammation, but inflammation does cause fever. A remedy which acted solely as a febrifuge, could not allay the inflammation. But a remedy which put a stop to the inflammation, might allay the fever.

The febrifuge property of the salicyl compounds is inadequate to explain their power to arrest the course of acute rheumatism. In virtue of that property they might allay the fever, but could not, without some other action, arrest the local inflammation.

But besides their febrifuge effect, the salicyl compounds have on the system no other action by which their power to arrest the course of acute rheumatism can be explained.

In health they have absolutely no action on the fibro-serous tissues of the motor apparatus.

When these tissues are inflamed from other than rheumatic causes, they are equally without action, and have no power to allay that inflammation.

But when they are the seat of rheumatic inflammation, no matter how acute, the salicyl compounds exercise over that morbid process a remarkable controlling influence.

Were it simply in virtue of their febrifuge properties that the salicyl

compounds cured acute rheumatism, their beneficial action would not be confined to that disease, but would be equally manifested in other febrile ailments: and that, we know, is not the case.

Again, the salicyl compounds have less febrifuge power than quinine and the cold bath. Were a febrifuge action that by which the cure of acute rheumatism is effected, quinine and the cold bath would be more serviceable than the salicyl compounds; but they have little or no anti-rheumatic action.

We are thus driven to the conclusion that the anti-rheumatic effects of the salicyl compounds are not to be explained by any action which they have on the system—febrile or non-febrile.

There remains only their action on the rheumatic poison.

As already remarked, there are two ways in which the salicyl compounds might so act as to deprive the rheumatic poison of its power to affect the system. They might supply to that poison the second factor requisite to its propagation; and so prevent it taking this from, and acting on, the fibrous tissues. Or they might destroy the rheumatic poison.

The former supposition is a very improbable one. It is difficult to find anything to say in support of it, except that it is possible. Against it, there is the same argument which applied to the case of quinine under similar circumstances. It would lead to the propagation of the rheumatic poison in the system during the whole period of administration of the drug, and to a sudden outbreak of rheumatic fever when its administration ceased.

The view that the salicyl compounds owe their anti-rheumatic effects to a destructive action on the rheumatic poison, has much more to commend it.

If that poison be a minute organism, there are good *a priori* grounds for regarding this explanation as at least a probable one; for the salicyl compounds are known to possess in a remarkable manner the power of destroying minute organisms. Salicylic acid was first introduced to notice as an antiseptic, *i.e.*, as an agent possessing the power to arrest those processes which are associated with, if not actually dependent on, the growth of minute organisms. For this reason, it has been administered in all diseases whose poisons were believed to be organized—diphtheria, scarlatina, typhoid fever, etc. Its administration in acute

rheumatism by the German physicians, was a pure piece of empiricism; and the results obtained matter of surprise rather than of expectation.

The views advanced in these pages as to the nature of the rheumatic poison, and as to the mode of action of the salicyl compounds, afford a scientific basis for this practice, and an adequate explanation of its success.

It has already been explained that I used salicin in the treatment of acute rheumatism more than a year before salicylic acid was brought into notice by Stricker and Riess; and that my employment of it was not a piece of empiricism, but a logical inference deduced from the views which I then held, and now advocate—first, regarding the nature of the rheumatic poison; and second, regarding the mode of action of quinine in intermittent and remittent fevers.

It need scarcely be pointed out that this view of the mode of action of the salicyl compounds, adequately explains their curative effects in acute rheumatism. It is the view, too, to which we have been driven by the failure of every other possible one to stand the tests of examination and inquiry. It alone stands these tests, and fulfils every requirement of a satisfactory theory. We accept it, not only because it does so, but because there is no alternative between it and blank ignorance.

The objection may be raised, that if the salicyl compounds possess the power to destroy minute organisms, their curative effects should be manifested in other ailments produced in the same way, and not be limited to acute rheumatism.

The answer is that already given to the same objection applied to the case of quinine:—poisons possessed of specific differences, may have these manifested, not only by their different effects on the system, but by the different effects which other agencies have on them

The fact that the salicyl compounds do not shorten the duration of other febrile maladies, is no proof that they do not owe their power to cut short acute rheumatism to their destructive action on the rheumatic poison.

The salicyl compounds form a numerous and remarkable series. There are in all some thirty or forty substances included in it. The chief of these are:—

	Formula.
Salicin	$C_{13}H_{18}O_7$
Saligenin	$C_7H_8O_2$
Saliretin	C_7H_6O
Salicylous acid (oleum spiræae) . .	$C_7H_6O_2$
Salicylic acid	$C_7H_6O_3$
Methyl salicylate (oil of winter green) .	$CH_3C_7H_5O_3$
Helicin	$4C_{13}H_{16}O_7 3H_2O$
Salicyluric acid	$HC_9H_8NO_4$

Though this table represents not a fourth part of the salicyl compounds, it serves to show the composition of those with which we shall have to deal. It will be seen that, with the single exception of salicyluric acid, which contains a little nitrogen, they are all composed of carbon, hydrogen, and oxygen.

The basis of the whole series is the radicle salicyl ($C_7H_5O_2$), a subtance which has never been isolated.

Of all the salicyl compounds, the only two which have hitherto been used in medicine are salicin and salicylic acid.

Salicin is extracted from the bark of various species of willow. It is a white crystalline substance, having a bitter taste. It is sparingly soluble in water.

When boiled for a few minutes with dilute sulphuric or hydrochloric acid, it is converted into glucose and saligenin, which latter may, after agitation with ether, be separated in a crystalline form. The same change takes place when salicin is allowed to remain in a solution of synaptase—the salicin is split up into saligenin and glucose. The solution strikes a deep blue color with ferric chloride. Salicin itself gives no such color.

If the boiling with the acid be continued for some time, the saligenin itself is destroyed, and there is formed a resinous substance called saliretin.

When salicin is acted on by a powerful oxidizing agent, such as chromic acid, the change does not stop at the formation of saligenin and sugar. These substances are also decomposed: the sugar producing formic acid, and the saligenin yielding a fragrant oily liquid, which is salicylous acid, or oleum spiræae.

Saligenin and saliretin also yield this oil, when treated with chromic acid. The change which takes place is simply one of oxidation; thus:—

$$\overbrace{2C_7H_8O_2}^{\text{Saligenin.}}+O_2=\overbrace{2(HC_7H_5O_2)}^{\text{Salicylous acid.}}+2H_2O;\ \text{and}$$

$$\overbrace{2C_7H_6O}^{\text{Saliretin.}}+O_2=\overbrace{2(HC_7H_5O_2}^{\text{Salicylous acid.}}.$$

Salicylous acid exists in nature in the flowers of the common meadow-sweet, the *spiræa ulmaria,* and may be got by distilling these flowers with water. It is generally prepared from salicin by the decomposing action of dichromate of potass. It is a colorless oily liquid, having a hot pungent taste, and the odor of the flower of the meadow-sweet. It combines with soda and potass to form salicylides. It strikes an intense violet color with ferric chloride.

If salicylous acid be fused with caustic potass, part of the hydrogen is liberated, and salicylic acid is formed:—

$$\overbrace{HC_7H_5O_2}^{\text{Salicylous acid.}}+KHO=\overbrace{KC_7H_5O_3}^{\text{Salicylate of potass.}}+H_2.$$

The same result takes place when salicylous acid is boiled in an alkaline liquid with oxide of copper.

Salicylic acid may be obtained in several ways. From salicin it may be formed by fusing it for some time with caustic potass. From the oil of winter-green it may also be formed by boiling it with caustic potass for a few minutes.

Now-a-days it is always prepared from carbolic acid by the action of caustic soda.

It occurs in needle-shaped crystals, sparingly soluble in cold, but very soluble in hot water. It combines with alkalies to form salts which are much more soluble. It gives a violet reaction with perchloride of iron.

When taken into the system, part of it passes away in the urine unchanged, and part becomes converted into salicyluric acid, a crystallizable colligated combination of glycocine, by a process analogous to that

by which, under similar circumstances, benzoic acid is converted into hippuric acid. Salicyluric acid also gives a violet reaction with the iron salt. By boiling with concentrated hydrochloric acid, it may again be split up into salicylic acid and glycocine.[1]

It has been asserted that salicin is converted into salicylic acid in the system; and Senator of Berlin has advanced the hypothesis that it owes its therapeutic properties to such conversion.

This view has been very generally accepted.

But from what has been said as to the chemical relationship of the different salicyl compounds, it will be seen that the conversion of salicin into salicylic acid is not the simple process that some would have us believe it to be.

To be converted into salicylic acid, salicin must be subjected to an amount of oxidizing force which is not likely to be brought to bear upon it in the system. We have already seen that boiling for a few minutes yields only saligenin; that by more prolonged boiling, saliretin is obtained; and that the action of a very powerful oxidizing agent, such as chromic acid, is required to carry the oxidation beyond this point, and to convert salicin into salicylous acid. Even then the process has not served to produce salicylic acid. To obtain this result, salicin must be fused for some time with a concentrated solution of three parts of caustic potass to one of salicin. Less vigorous measures lead only to the formation of saligenin, saliretin, and salicylous acid. On chemcial grounds, therefore, we should expect the oxidation of salicin in the system to result in the formation of these substances, rather than of salicylic acid.

"But," says Senator, "the observations of Latheran and Millon, and of Ranke, show that salicylic acid is so converted." I do not think they do: for the tests on which these observers relied, and which Senator regards as adequate, are not sufficient. After ingestion of salicin, they found that the urine invariably gave a violet reaction with perchloride of iron, and that crystals of what they regarded as salicylic acid were found in the urine. But neither this reaction nor the crystalline form is peculiar to salicylic acid. Salicylous acid gives the same reaction, and saligenin gives a deep blue which very closely resembles

[1] Miller's Elements of Chemistry.

it. It is not shown that the crystals which they got were not those of saligenin. Moreover, in one of his experiments, Ranke found crystals of undecomposed salicin in the urine.

Dr. Spencer[1] of Bristol analyzed 1300 c.c. of the urine of a man who had taken 120 grains of salicin. "The crystalline extract consisted of an acid body supposed to be salicylic acid along with salicyluric acid. The acids could not be separated from one another, nor the amount of each determined, as no good method of separation is known; but there was no doubt that some of the crystals contained nitrogen. Now, it may be fairly computed that the patient had taken 120 grains of salicin in the period during which the 1300 c.c. of urine were passed. 120 grains of salicin might yield, if all of it was converted into saligenin and glucose and thence into acid, 50 grains of salicylic acid. How much salicylic acid this patient excreted we cannot tell. But we know that only about 12 grains of mixed acid crystals were recovered from a quantity of urine, representing 50 grains of salicylic acid. And this 12 grains represents glycocine as well as acids."

But here, as in the experiments of the German observers, what proof have we that salicylic and salicyluric acids were excreted? It is not shown that the crystals were not saligenin; and that the nitrogen which some are said to have contained, was not derived from urea or uric acid. Moreover, supposing that the crystalline matter did consist of salicylic and salicyluric acids, what proof have we that these acids were formed in the body, and not from salicylous acid or saligenin during the process requisite to the formation of an ethereal extract? The only certain point is, that from 120 grains of salicin there was not produced enough salicylic acid to exercise any possible therapeutic effect.

The salicyl compounds are so recent an object of therapeutic interest, and the changes which any one of them undergoes in the system so little understood, that anything like dogmatic assertion should be avoided.

I do not say that salicylic acid *cannot* be formed from salicin in the system; but I do say that saligenin, saliretin, and salicylous acid, are

---

[1] The Chemical and Therapeutic Relations of Salicin and Salicylic Acid, by W. H. Spencer, M.A., M.D., Senior Physician, Bristol Royal Infirmary, etc. (Transactions of Bristol Medico-Chirurgical Society, 1878.)

more likely to result from its decomposition, and serve equally well to explain those results which have been regarded as indicative of the presence of salicylic acid.

All the salicyl compounds, except salicin, give a blue or violet reaction with ferric chloride. Saligenin, saliretin, and salicylous acid are easily formed from salicin: salicylic acid with difficulty. The reaction got by adding ferric chloride to the urine of one taking salicin, is most likely due to the presence of saligenin. Even those who have tried to prove that this reaction is due to the presence of salicylic acid, have succeeded only in demonstrating that, after ingestion of salicin, that acid is not formed in quantity sufficient to produce any therapeutic effect.

Chemical evidence does not support the view that salicin is converted into salicylic acid in the system.

But the question has also a therapeutic aspect. For if it be the case, as Senator asserts, that salicin "owes its therapeutic virtues" to its conversion into salicylic acid, then ought both drugs to exercise the same action on the system. But this is in direct opposition to clinical experience; for observation shows that salicin possesses therapeutic properties not possessed by salicylic acid; and that salicylic acid gives rise to symptoms which do not follow the administration of salicin.

1. Salicin is a bitter tonic, and may be prescribed with great advantage as such. Given in the dose of ten grains three or four times a day, when the use of such a tonic is indicated, it stimulates the appetite, and produces a generally tonic action such as frequently follows the administration of quinine. In the debility of the early stage of convalescence from acute diseases, it is very useful.

Salicylic acid has no tonic action. It tends rather to produce nausea and depression.

This different effect of the two drugs is evidenced by a fact noted by observers who have used them both in the treatment of acute rheumatism—that cases treated by salicin are less debilitated at the end of the attack, and convalesce more rapidly, than those treated by salicylic acid.

2. The quantity of salicylic acid requisite to the cure of acute rheumatism often produces great disturbance of the system. This disturbance shows itself chiefly in the brain and the heart.

The brain. Numerous cases have been recorded in which the administration of salicylic acid has been followed by delirium, more or less violent. Few who have had much experience in its use can have failed to have met with this effect. Sometimes the cerebral disturbance is really alarming.

It was supposed by Murchison and others that this symptom was due to a disturbing action of the acid on the renal secretion, and consequent retention in the blood of excretory products. But that hypothesis has been set aside by the fact that delirium has been noted in cases in which there was no interference with the action of the kidneys, and no retention of excreta.

It has also been thought that this disturbance might be due to the presence of carbolic acid, consequent on imperfect purification of the drug. There is reason to believe that in some of the earlier reported cases this may have been so; but there is now no doubt that such an explanation applies only to a few; and that cerebral disturbance may be produced by salicylic acid whose purity is undoubted.

Without causing actual delirium, salicylic acid may give rise to nervous prostration, a sense of weight and oppression in the head, and a feeling of general misery which is very distressing.

Salicin gives rise to no such untoward effects. "I have never seen salicin, even when given in very large dose, produce delirium," says Dr. Sydney Ringer, who has made very extensive observations with it.

The *Lancet* for July 31, 1880, contains a clinical abstract of a half-year's hospital work by Dr. Charteris, Professor of Materia Medica at the Glasgow University, and Physician to the Glasgow Royal Infirmary.

The cases of rheumatic fever are thus referred to:—

"They were all treated with salicin in twenty-grain doses every two hours, with invariably satisfactory results. In all the cases the patient was free from pain in twenty-four hours, and the temperature was normal in forty-eight. When this result had been attained, the salicin was given in smaller doses, twenty grains every four hours for the first day, and afterwards the same quantity every six hours for two days, when it was stopped and a tonic administered. Dr. Charteris had invariably followed this line of practice for the last four years, and could not speak too highly of the remedy. He had never known it cause delirium or weakening of the heart's action. On the contrary, the relief

was marvellous and the recovery materially hastened. On an average, the patient was able to leave bed within seven days after admission, and no other treatment he had tried could give any result at all to be compared with this. In former years he had tried for comparison the salicylate of soda, but it caused temporary deafness, headache, and insomnia, and he had latterly entirely abandoned it, being more than satisfied with the action of salicin."

Dr. Flint[1] says that "salicylic acid in some instances has produced alarming toxic effects, and even death. No such effects have been observed to follow salicin; and its controlling influence over acute rheumatism is probably not less than that of the salicylic acid."

I myself have used salicin more frequently and more freely than salicylic acid, but have never found it cause delirium. I have on numerous occasions seen such disturbance produced by salicylic acid.

The only unpleasant effects which I have found follow large doses of salicin, are such tinnitus, partial deafness, and headache, as frequently result from the administration of quinine.

The heart. Symptoms of cerebral disturbance are not the only toxic effects of salicylic acid. The heart also suffers. The cardiac symptoms are much less obvious than the cerebral, and are, therefore, more apt to escape notice, unless they exist in a marked degree.

The action of salicylic acid on the heart is essentially depressing. The evidence of this is feebleness and increased frequency of the pulse and cardiac action: the sounds are wanting in tone, and the apex beat becomes less distinct. The general prostration which accompanies this condition, varies with the extent of the cardiac depression. If this is very marked, the patient's state may cause alarm and anxiety.

If there be at the same time enough cerebral disturbance to cause wandering and delirium, the patient has much the aspect of one suffering from typhoid depression.

With the omission of the drug, the normal heart regains its tone. But if the muscular substance of that organ be at all weakened or softened from other causes, such as rheumatic carditis, typhoid fever, etc., the depressing effect of the salicylic acid may be serious, and possibly hasten a fatal termination.

---

[1] Practice of Medicine.

This action on the heart is not produced by salicin. I have never seen anything approaching it, even from large and frequent doses.

If further evidence were wanted to show that salicin does not owe its therapeutic effects to its conversion into salicylic acid, we should find it in the fact that when a man is suffering from the toxic effects of the acid—while he is depressed from its action, and still under its influence—salicin may be freely administered with benefit. Under its use, the depressing effects of the salicylic acid disappear. This could not be the case if the salicin owed its therapeutic virtues to its conversion into salicylic acid.

CASE XX.—A man, aged 40, who had twice previously, at 20 and 26 years of age, suffered from acute rheumatism, had a third attack in June, 1878. When seen, on the 4th day of illness, both wrists and the right knee were swollen and painful; tongue furred; perspiration acid; urine high-colored and depositing urates; pulse 100; temperature 101.4°; bowels moved by medicine; heart normal. To have twenty grains of salicylate of soda every hour, till six doses have been taken, and after that, every two hours.

He began to take his medicine at noon. In the evening I was sent for to see him. He was better, so far as the rheumatic symptoms were concerned. The joints were less swollen and not so painful; the pulse was up to 120, and was small and feeble; the temperature had fallen to 99.8°. But his general condition was much changed. His wife stated that he complained of the medicine making him feel depressed and uncomfortable after the third dose, and that after the fifth he began to wander. When seen by me, after having taken in all 140 grains of the salicylate, he had the appearance of one suffering from *delirium tremens*. His expression was anxious; he was wandering and talking nonsense, fancying that there was some one under his bed, and behind the window curtains. He knew me perfectly, but, though I was quite alone, asked who that was that I had with me. He had no recollection of having seen me in the morning, and thought that I had come straight to him from Ireland, where I had been some weeks previously. The urine was high-colored, and free from albumen; he was perspiring freely. The heart's sounds were wanting in tone; there was no abnormal *bruit*.

The salicylate was omitted, and he was ordered instead, thirty grains of salicin every two hours.

On the following morning he was much better. Had wandered during the night, but fell asleep about half-past three; slept for three hours, and afterwards had short snatches. When seen at 9 a.m., was quite rational, but feeling stupid and confused. Had no recollection of having seen me yesterday evening; but quite remembered the morning visit. Pain in joints gone; pulse 100; heart's sounds improved in tone; temperature 98.5°. To have thirty grains of salicin every three hours.

He got rapidly well.

CASE XXI.—A woman, aged 30, was laid up with her second attack of acute rheumatism. Right ankle and knee and left elbow swollen and painful; acid sweats; pulse 104; temperature 102.1°; heart unaffected. She was ordered twenty grains of salicylate of soda every two hours. On the following day, after having taken 180 grains of the salicylate, the rheumatism was better; the joints were less swollen and scarcely at all painful, except on firm pressure; and the temperature had fallen to 100°: but the pulse was 120, small and feeble; she complained of nausea, and a sense of misery and depression, and thought the medicine "did not suit her." The heart's impulse was barely perceptible, and the sounds wanted tone. The salicylate was omitted, and she had instead thirty grains of salicin every two hours.

On the following day it was reported that she had slept well all night, having wakened up only twice. On each occasion she took a powder. Took seven in all, equal to 210 grains of salicin. Pain gone; the joints not even tender to touch, but feeling stiff; pulse 96, of better volume; heart's sounds pretty good; temperature 98.8°. To have thirty grains of salicin every four hours. She continued to take it so for several days, and made a perfect and rapid recovery.

CASE XXII.—A medical friend suffering from subacute rheumatism, asked me to see him. He had been taking salicylate of soda, which, though it did good to his rheumatism, produced cardiac depression. The following is his own statement: "Both drugs relieved the pain, tenderness, and swelling, when taken in full doses frequently

repeated. But the salicylate, which I employed first, produced some very unpleasant effects. After taking several twenty-grain doses, a copious perspiration was produced; the strength of the pulse was very distinctly diminished, while its frequency was increased; and a feeling of most uncomfortable depression, with singing in the ears, ensued. Indeed, I hardly knew whether the disease or the remedy was the preferable. Salicin, on the other hand, improved the tone of my pulse and digestion, and relieved the pains more rapidly. To my mind, one of the great merits of salicin is the absolute safety with which large doses can be taken. In the course of one period of twenty-four hours I swallowed an ounce of it with nothing but benefit."

In this case the dose of salicylate of soda was twenty grains every two hours. While suffering from the depressing effects of this, salicin was given in larger dose, with the result stated.

These are not isolated cases; but they serve as well as a dozen would, to illustrate a point of much importance in practical therapeutics—*that salicin may be freely administered while the system is still depressed from the toxic action of salicylic acid, and that under its use the rheumatic and the salicylic symptoms both disappear.*

Did salicin owe its effects to its conversion into salicylic acid, such a result would be impossible. The rheumatism would be cured, but the symptoms referable to the salicylic acid would be kept up, so long as salicin continued to be administered.

Senator recognizes the superiority of salicin over salicylic acid in this respect, and the immunity from unpleasant symptoms enjoyed by those who take it. This he endeavors to explain by supposing that only a part of the salicin is converted into salicylic acid, and that the conversion takes place slowly and gradually, so that there is not at any time in the system enough of the acid to cause its toxic effects.

But if that be so, what becomes of his theory that the therapeutic effects of salicin are due to its conversion into salicylic acid? and how is the rapid anti-rheumatic action of salicin to be explained? If that acid be formed from salicin only slowly and gradually, then salicin ought not to have the decidedly curative effect in acute rheumatism that Senator acknowledges it to possess; for salicylic acid is so rapidly eliminated from the system, that its slow and gradual formation would not suffice to keep up its therapeutic effects. The quantity of acid requisite

to the production of a decided anti-rheumatic effect is not less than that which suffices to produce its toxic effects in susceptible subjects; and yet such persons may have their rheumatism cured by large doses of salicin, without any such unpleasant symptoms as follow the use of salicylic acid. Evidence of this we have in the cases which have been given.

When once the depressing effect of the acid had been produced, a moderate dose would suffice to keep it up; but even the quantity requisite for that purpose is not to be got from the administration of salicin in even larger dose than suffices to ensure its anti-rheumatic action.

Moreover, if salicin owes its therapeutic effects solely to its conversion into salicylic acid, and if "only a part of the salicin is converted into salicylic acid," a large dose should not be more efficacious than one half the size. If when fifteen grains are administered, only ten are in a given time converted into salicylic acid, no more than ten would in the same time be so converted, if we were to give thirty; and fifteen grains would be as efficacious a dose as thirty. But that is in direct opposition to clinical experience. It is a fact that salicin given in large dose cures acute rheumatism more quickly than the same remedy given in smaller quantity.

The therapeutic evidence, even more decidedly than the chemical, is opposed to the view that salicin owes its anti-rheumatic properties to its conversion into salicylic acid.

The fact is, that this hypothesis of Senator's was advanced at a time when men's minds were in a state of excitement about the new treatment of rheumatism, and when little or nothing was known by the mass of the profession about the chemistry and therapeutics of either salicin or salicylic acid.

Men did not stay to criticise the grounds on which the hypothesis was based; but, struck by its simplicity, accepted it at once, and without hesitation, on the authority of Senator.

There is ample evidence that Senator came to too hasty a conclusion; that his hypothesis is one which cannot be maintained; and *that salicin and salicylic acid, while exercising a like action on the rheumatic poison, have an essentially different action on the system.*

The really important question for us to determine is, not so much what changes salicin and salicylic acid undergo in the system, as how

each produces its anti-rheumatic action. There is little practical good to be got from speculating on the former point: the latter is of vital importance. But in order to come to any satisfactory conclusion regarding it, it is necessary that we should have some definite idea of the nature and mode of action of the rheumatic poison. So long as we are in the dark as to the nature of the rheumatic process, it is vain to inquire how the salicyl compounds arrest its course.

But, if the views advanced in these pages be correct—if it be the case that the rheumatic poison is a minute organism, and that the salicyl compounds owe their anti-rheumatic effects to their destructive action on this poison—then the hypothesis of Senator is as unnecessary as unreliable. For if such be the mode of action of these compounds, it is evident that, while each may have a different action on the system, they may all have the same action on the rheumatic poison.

Instead of being regarded as the only salicyl compound capable of destroying the rheumatic poison, and exercising a consequent anti-rheumatic action, salicylic acid is to be looked upon as only one of a series, comprising salicin, saligenin, salicylous acid, saliretin, helicin, and many others, any one of which may have anti-rheumatic properties.

The basis of the whole series is the radicle salicyl. If any one of the series were to be indicated, on theoretical grounds, as being *the* anti-rheumatic agency *par excellence*, it would be this radicle. As a necessary consequence of such a view, all the salicyl compounds would be regarded as possessed of anti-rheumatic properties. But as the radicle salicyl has never been isolated, and cannot be obtained in a separate form, this point must continue to be matter of speculation.

My own belief is that the whole of the salicyl series is possessed of anti-rheumatic properties; and that, in this respect, no one of them is likely to have any great superiority over the others. From observations made with saligenin and salicylous acid (oleum spiræae) I feel confident that they possess this action. But the practical difficulties in the way of obtaining and administering these, are a bar to their use. Salicin and salicylic acid are the two which are at once the most easily obtained and the most convenient for administration. They are the only two which, up to this time, have been used in medicine.

It has been clearly shown that in small doses neither remedy is of much avail. To get its full beneficial effects in acute rheumatism, each

requires to be given in large and frequently repeated dose. The explanation is obvious. The rheumatic poison is a minute organism which is propagated in, and acts on, the fibrous tissues of the motor apparatus of the body. It is, of course, carried about in the blood. The salicyl compounds act by destroying this poison. For its complete destruction a certain quantity is necessary. The sooner this quantity is introduced into the blood, and so brought to bear on the poison, the more rapid will be the cure of the rheumatism. The exact quantity required for this purpose will vary in different cases, and cannot in any one be determined beforehand.

Such being the mode of action of the salicyl compounds, it is obviously of less importance to determine with how little their anti-rheumatic effects may be got, than it is to determine how much can, in a given time, be received into the system with impunity. The larger the quantity which can be brought to bear upon the rheumatic poison, the more speedy will be the arrest of the rheumatic process. To saturate the system with the remedy is, therefore, the object in view: and the question for consideration is how this saturation may be most speedily and safely accomplished—or how, in other words, the rheumatic poison may be most rapidly and effectively destroyed, without injury to the system.

Salicin and salicylic acid being the only salicyl compounds used in medicine, the question narrows itself into a consideration of the respective safety of these two drugs.

On the rheumatic poison they exercise the same destructive action. Senator, indeed, has asserted that the anti-rheumatic action of salicin is more slowly produced than that of salicylic acid. Such an opinion was the necessary outcome of his view that it owes its action to its conversion into that acid, and that such conversion is partial and slow: but this view we have seen to be untenable. In my experience, there is, in rapidity of action, very little to choose between the two. The chief question is, "Which produces its destructive action on the rheumatic poison with least disturbance of, and danger to, the system?" On this point there can be no doubt. The quantity of salicylic acid requisite to the cure of acute rheumatism, often gives rise to so much disturbance of the brain and heart, that the administration of the drug cannot be continued without risk. Such disturbance does not follow the ad-

ministration of salicin, which may be given freely, and without fear of any untoward result attributable to it. It is impossible to saturate the system with salicylic acid without risk. It may be saturated with salicin with impunity. Of how much importance it is that such saturation should be effected not only speedily, but without the production of cardiac depression, we shall see when considering the treatment of the heart complications of rheumatism.[1]

---

[1] Salicin is prepared from the bark of different species of willow. The bark is removed in spring, when it contains the largest quantity of the bitter principle, so that the quantity in the market during the summer represents all that is to be had till the following spring. Previous to the publication of my original paper (March, 1876), salacin was rarely prescribed, and was kept by chemists chiefly as a curiosity. There was but a limited quantity in the market. The price at that time was two shillings an ounce. After my paper appeared it speedily rose to six, eight, and even twelve shillings; and ultimately ceased for a time to be quoted in the druggists' monthly lists. The demand far exceeded the supply; and no more bark could be had till next spring. And yet chemists continued to supply it. They could not have given pure salacin, for it was not to be had. The combination of rise in price, great demand, and insufficient supply, led to the usual result of such a combination—adulteration. The substance used for this purpose was boracic acid; and much of what was sold as salicin was, I have been informed, a mixture of boracic acid and salicin, or even of boracic acid and quinine. To this adulteration of the drug was no doubt due the unsatisfactory results which some got from it at the time to which I refer.

The following interesting letter I received from South Africa not long after the publication of my original paper on the Treatment of Acute Rheumatism by Salicin.

"*Port Elizabeth, South Africa, April 14th*, 1876.

"DEAR SIR,—I have seen with much interest your papers in *The Lancet* on the Treatment of Rheumatism by Salicin, and thought that the following story might be welcome.

"In 1861, I was district medical officer in Hope Town, on the banks of the Orange River, not far from the now celebrated diamond-fields. The town is situated in one of the high plateaus of South Africa, and the country is occupied by a race of nomadic Dutch Boers, who live in waggons or tents, traveling about from place to place, as the rains, or rather occasional thunder-storms, filled the natural hollows. When these are dried up, the farmers are obliged to fix their abodes on the banks of the river.

"The temperature in summer is very high, and the dryness of the atmosphere so great that surgical instruments or fire-arms never rust. The winter, with its clear bright sun and cool temperature, is most exhilarating. You can imagine that a doctor's life in such a region must indeed be a sinecure. On one occasion, however, I was sent for to visit the wife of a Dutch Boer, who was said to be very ill. I found my patient of the usual Dutch build, *informe ingens*, lying on a camp-bed in a little tent, where the heat was something

terrific; a naked bush child trying to fan away the cloud of flies which was tormenting my poor patient, bound hand and foot, I may say every joint, in the cruel bonds of as fierce an attack of rheumatic fever as I ever saw. She was perspiring profusely. The time that has elapsed has obliterated my memory of pulse, temperature, and heart complication. I prescribed the usual alkaline mixture, with calomel and Dover's powder at bedtime, and rode away.

"Some two months after, my former patient entered my surgery, looking remarkably well, and I very naturally congratulated myself and her that she had recovered so completely. I was quite taken aback when she bluntly told me that my physic hadn't helped her a bit. On inquiring what had helped her, she said that the old Hottentot shepherd had made her a decoction of the shoots of the willows which grow on the banks of the river, and that after taking this for a few days she began to get better.

"Your papers in *The Lancet* brought the picture of the stout Dutch woman back to my memory. I afterwards learned that a decoction of willow-tops is a favorite remedy for fever, and what the Boers and native Hottentots call 'sinken kors' or rheumatic fever.

"Trusting that this remedy which you have scientifically thought out may prove as beneficial as the 'willow-tea' selected by these children of nature,

'I remain yours very truly,

"FREDK. ENSOR,

"Surgeon to Provincial Hospital, Port Elizabeth."

CHAPTER XVII.

THE TREATMENT OF VASCULO-MOTOR RHEUMATISM.

In its general pathology, rheumatism of the heart is identical with rheumatism of the joints. The poison is the same; the textures which chiefly suffer are the same; and there is no difference in the mode in which the poison acts. The morbid process is, therefore. fundamentally the same in both.

Such being the case, it is natural to suppose that both should yield to the same treatment, and that the beneficial results which follow the administration of the salicyl compounds in rheumatic inflammation of the joints, should equally follow their administration in similar inflammation of the heart. And such no doubt would be the case, if the heart were in all respects similarly situated to a joint. But it is far from being so. For though, in its general pathology, rheumatic inflammation of the former is identical with similar inflammation of the latter, there exist between them several important differences, which it is necessary for us to recognize, if we would form a just estimate of the relative value of the salicyl compounds in the treatment of each. For the formation of such an estimate, we must not only have accurate views regarding the general pathology of rheumatism, but must also be alive to the special peculiarities of the disease as it presents itself in th vasculo-motor system.

In both heart and joints it is the fibrous textures which suffer first and chiefly. In both heart and joints these textures have the same duties to perform—they regulate movement, and resist strain. The chief difference to be noted between them, is in their relative functional activity. A joint acts only occasionally, never for more than a few hours in succession, and gets complete rest for many hours every day. The heart gets no rest, but beats on by day and by night, without cessation or repose.

This physiological difference exercises a vast and important influence

in disease, and especially in such acute inflammation as that which now engages our attention.

To an inflamed organ, rest is of the utmost importance. If a joint is inflamed, it becomes painful; motion increases the pain; instinctively we give it rest, and its function is in abeyance till the inflammation is at an end. If a man suffering from rheumatic inflammation of the knees and ankles were to persist in going about as usual (supposing such a thing to be possible), he would thereby prevent recovery. The salicyl compounds might be given so as to destroy the rheumatic poison, but the continued exercise of the inflamed textures would keep up the inflammation, independently of the cause which originally set it agoing, and they would probably not recover till they got rest.

When the heart is inflamed, it gets no rest: no matter what the consequences to itself, its work has to be done; and done it is, so long as life lasts. The fever of the accompanying joint affection, as well as the inflammation of its own textures, causes increased excitability and increased frequency of action, so that, instead of rest, there is greater activity—instead of its function being in abeyance, it is exalted. This it is which makes the chief difference between the results of rheumatic inflammation of the heart, and similar inflammation of a joint; and this it is which makes the former so much less amenable to treatment.

In both heart and joints the rheumatic poison causes inflammatory thickening of the fibrous textures; but in the latter, the inflamed tissue gets rest, and the morbid change is temporary; in the former, rest is unattainable, and the morbid change is permanent. It is not in the nature of the morbid process, but in its results, that lies the difference between the two. In considering the question of their respective amenability to treatment, it is essential that this should be borne in mind, and that the effects attributable to the inflammatory process, should be distinguished from those directly due to the action of the rheumatic poison.

The destruction of the rheumatic poison *must* put a stop to its direct action on the heart as well as the joints. But to do this, is quite a different thing from removing the morbid products resulting from that action. It is a step, and a very necessary one, towards that end; but something more is requisite to its complete attainment. For this, it is requisite that the inflamed textures should have rest. In the joints

this is easily got; in the heart it is unattainable. The inflamed valves continue to be strained, their roughened surfaces continue to rub, the friction keeps up the irritation; the damage which has been done by the rheumatic poison is thus increased by some of its effects, and restoration to the normal is rendered all but impossible.

Though the heart affection very seriously complicates the rheumatic attack during whose course it occurs, it is not in any way, or in any case, to be regarded as an *accidental* complication, but always as part of the disease, and as being induced in exactly the same way as the joint inflammation.

If the heart suffer, it does so for the same reason that a given joint suffers—because its textures contain the second factor requisite to the propagation and action of the rheumatic poison. If the heart contain this second factor, it does so naturally, and before the rheumatic poison gains entrance to the system. It is, therefore, in danger from the very first: and, theoretically, there is no reason why it should not give evidence of disturbance at as early a period as the joints. Practically, there are three reasons why it should not do so:—

1. The joints are much more numerous; and the chance of one or more of them suffering first, is correspondingly great.

2. The amount of fibrous tissue in a given large joint, is much greater than that which exists in the heart. The chance of the locomotor apparatus being the first to suffer is thus increased to a corresponding degree.

3. The symptoms of rheumatic inflammation of the fibrous textures of a joint, are prominent from the commencement of the attack: those of rheumatic inflammation of the fibrous textures of the heart, are more tardily developed, and are not apparent till these textures have suffered for some time.

Let us consider this third point more carefully, for it is an important one.

In both joint and heart, the fibrous tissue is the part which suffers first. In the joint the inflammation extends from the fibrous textures to the synovial membrane; in the heart, from the fibrous rings and valves to the endo- and peri-cardium. Before the synovial membrane becomes affected, there is already pain, tenderness, and all the necessary evidence of inflammation of the fibrous textures. But, until the mis-

chief has extended to the endo- or peri-cardium, there is no such evidence, and no possibility of diagnosing the existence of inflammation of the fibrous textures of the heart; for such inflammation gives rise to no symptoms or signs before some change has taken place in one or other of these membranes.

The signs of endocarditis (to which for the present we shall confine our attention) are those of roughening of the endocardial surface of a valve; but such roughening is not produced by the direct action of the rheumatic poison on the lining membrane: it is the indirect result of a prior inflammation of the subjacent fibrous tissue.

It follows from this, that there is a stage of the endocarditis which precedes the roughening of the endocardial surface, and precedes, therefore, the earliest evidence of the heart affection. In other words, rheumatic endocarditis cannot be diagnosed till the ailment has existed for one or more days. An endocarditis whose physical signs first become apparent on a Wednesday, has almost certainly begun on Monday or Tuesday, if not sooner.

If the rheumatic poison affect a joint and the heart simultaneously, pain, the earliest evidence of joint inflammation, will precede, possibly by some days, the endocardial blow, which is the earliest indication of the heart being affected. The rapidity of development of the endocardial murmur will vary with the acuteness of the attack; but in any case, its comparatively late development will make the cardiac inflammation appear secondary to that of the joints, though the two may in reality have originated simultaneously.

Pain, the earliest and chief evidence of rheumatic arthritis, exists from the commencement of the attack; but an endocardial murmur, the most reliable, and generally the only, evidence of endocarditis, is not an early sign: it marks the attainment of that stage of the disease at which the lining membrane becomes roughened.

Thus it happens that by the time an endocarditis is diagnosed, serious damage has already been done to the heart. The roughening which produces the endocardial blow is caused by rubbing of the swollen valves: the roughening itself leads to the deposition of lymph on the affected surface, and to increase of friction. And so the mischief is kept up, independently of the action of the rheumatic poison.

When the heart suffers in acute rheumatism, it nearly always does

so at an early stage of the disease. In this respect, it resembles the joints. No matter how prolonged a rheumatic attack may be, all the joints which suffer during its course, are generally affected within the first week or ten days. Some of them may suffer more than once; but joints not affected up to that time are likely to escape altogether.

So it is with the heart. If it suffer at all, it generally does so during the course of the first week. If that is passed over in safety, the heart is likely to escape. And the reason is obvious. What renders the heart or a joint susceptible to the action of the rheumatic poison, is the presence in its textures of the second factor requisite to the propagation and action of that poison. If the heart contain this second factor at all, it does so from the commencement, and is in danger from the first moment that the poison gains entrance to the system.

The points to be chiefly borne in mind are:—

1. That the heart, if it suffer at all in acute rheumatism, suffers early.

2. That the part first affected is the fibrous structure of the rings and valves.

3. That the endo- and peri-cardium suffer secondarily, and, therefore, later.

4. That, prior to its extension to their endocardial covering, inflammation of the fibrous textures of the valves cannot be diagnosed.

5. That injury to the valves, though indirectly due to the action of the rheumatic poison, is directly and chiefly attributable to the mechanical rubbing of one part against another.

6. That roughening of the endocardial surface is developed only after the inflammation of the fibrous textures has reached a certain stage—that of thickening.

7. That such roughening is no essential part of the action of the rheumatic poison; but a change incidental to the peculiar function and construction of the affected tissues.

8. That rest to an inflamed organ is of the first importance to its recovery.

9. That this condition is unattainable in the heart.

Keeping before us these special peculiarities of rheumatic inflam-

mation of the heart, we are in a position to take up the important question of the action of the salicyl compounds in such inflammation.

The question has naturally two aspects—a prophylactic, and a curative.

1. Do the salicyl compounds tend to prevent heart complications in acute rheumatism?

2. Do they have a curative action on these after they have occurred?

We shall first deal with the prophylactic aspect of the question.

That a remedy which rapidly cures acute rheumatic inflammation of the joints, should tend to ward off, if not prevent, the heart complications which so frequently accompany such inflammation, is a reasonable supposition. And sanguine hopes were at one time entertained that such an action the salicyl compounds would have.

These hopes have not been realized. Numerous cases have been recorded in which heart complications have appeared in the course of acute rheumatism, after the salicyl treatment had been established.

How is this to be reconciled with the views advanced, first, as to the pathology of rheumatic inflammation of the heart; and, second, as to the mode of action of the salicyl compounds?

If it be the case that rheumatic inflammation of the heart is produced in the same way as rheumatic inflammation of a joint; and if it be the case that the salicyl compounds destroy the rheumatic poison, should not these compounds, in virtue of that action, ward off and arrest the course of heart inflammation, as they ward off and arrest the course of inflammation of the joints? Theoretically, yes; practically, no. And "no" for the following reasons:—

In order to get the full beneficial action of the salicyl compounds in rheumatism of the joints, they have to be given in large doses frequently repeated; and their action has to be kept up for a time after the pain is abolished and the fever allayed. In other words, the rheumatic poison has to be overwhelmed, as it were, by the agency which destroys it; and the system has to be saturated for some time with this agency to render that destruction complete. If the salicyl compounds be not given in sufficient dose, or for a sufficient length of time, a certain quantity of the poison evades destruction, and may produce mischief.

In many of the recorded cases in which heart mischief appeared

during the salicyl treatment, its occurrence was fairly attributable to the inadequate protection of a small dose. From what is observed in the joint affection, we know that frequently repeated full doses are requisite to a rapid cure, and the prevention of renewed arthritic attacks. The heart is, in this respect, in the same position as a joint, and runs the same risk of suffering while the blood contains the rheumatic poison.

But a more constant, and probably more potent agency intervenes, not actually to diminish any prophylactic action possessed by the salicyl compounds, but to render that action less apparent, and to lead us to underrate their usefulness in that respect.

We have seen that, in the heart, the rheumatic poison acts primarily on the fibrous textures of the rings and valves, and only secondarily on the lining and investing membranes. We have also seen that inflammation of these fibrous textures gives rise to no symptoms or physical signs, and that not till the membranes are affected can the disease be diagnosed. In other words, the rheumatic poison is acting on the heart for some time before there is any evidence of its doing so. The first indication of its action on the endocardium, is the development of an endocardial blow. But before this can be developed, there take place—

1. Cellular infiltration of the fibrous textures of the valve, and consequent elevation of its endocardial covering.

2. Rubbing of one segment against another.

3. Roughening of the endocardial surface consequent on such friction.

All that takes time—how much it is impossible exactly to say—but probably not less than from one to two days: so that before an endocarditis is detected, it has probably existed for at least thirty-six hours.

If the salicyl compounds be given to a man just as the fibrous textures of the heart are beginning to suffer, they are not given in time to stop the action of the rheumatic poison on them, or to prevent proliferation of their cellular elements; they are not given in time, therefore, to prevent swelling of the valves, and rubbing of their segments, and, consequently, not in time to prevent those changes on the endocardial surface which lead to the signs of endocarditis.

The development of an endocardial murmur two days after the com-

mencement of salicyl treatment, seems, on a superficial view of the matter, to indicate that this treatment possesses no power to prevent cardiac complications. More careful inquiry shows this conclusion to be hasty, and probably erroneous. For, first, the signs of endocarditis are not developed till the disease has already existed for one or two days; and, second, as we know from what is observed in rheumatic inflammation of the joints, it takes a day or two to get the full action of the salicyl compounds.

A man may begin to take these compounds on Monday, and on that day the heart's sounds may be quite normal. On Tuesday his joint inflammation may be much better; but there may be a distinct endocardial blow. That enough of the salicyl compound had been taken to check the rheumatic process, is evidenced by the improvement in the joint inflammation; that what served to allay the joint inflammation, did not suffice to save the heart, is evidenced by the development of the endocardial blow.

From the coincident decline of the arthritic, and development of the cardiac symptoms, the inference might naturally be drawn, and has in several cases been drawn, that the salicyl compounds have no power to prevent cardiac complications in rheumatism. But a careful examination of all the circumstances of the case would lead to a more cautious, if not different, conclusion.

Any prophylactic property possessed by the salicyl compounds in rheumatic inflammation of the heart, must be due to their destructive action on the rheumatic poison. They save the heart by destroying the poison. But this saving action cannot be got unless they are given in adequate quantity *before the poison has begun to act on the heart*, for with the commencement of morbid change in that organ, terminates the period of possible prevention. Inflammation of the fibrous textures of the heart exists, as we have seen, for one or two days before it can be diagnosed. It takes also from one to two days to introduce into the system enough of the salicyl compounds to destroy the rheumatic poison, and to enable us to get the benefit of the prophylactic action which such destruction implies. The rheumatic poison may have begun to act on the heart before the salicyl treatment was commenced, but its symptoms may not be developed for twenty-four hours later. The morbid process had precedence of the treatment. It had a

clear lead of twenty-four hours; and prevention was out of the question.

But even if the start were fair and equal—even if the salicyl treatment commenced at the same moment that the rheumatic poison began to act on the fibrous textures of the heart—the morbid process would still have the advantage, for probably twenty-four hours would elapse before there could be introduced into the system the quantity of the salicyl compounds requisite to the destruction of the poison. During these twenty-four hours the rheumatic poison would have time and opportunity to cause such change in the fibrous textures as would lead to thickening of the valves, to consequent friction of their segments, and to the development of the symptoms of endocarditis; while the continued activity of the inflamed tissues would prevent the decline of the inflammation, which might otherwise be expected to follow the destruction of the rheumatic poison.

It is impossible to state with exactitude, either the time which, in a given case, must elapse between the commencement of cardiac inflammation and the development of an endocardial blow, or the quantity of the salicyl compounds requisite to destroy the rheumatic poison. The former must vary with the acuteness of the attack; the latter with the amount of poison in the system at the commencement of treatment, and with the stage of the disease at which treatment commences.

In no given case can we positively assert that the absence of heart complications is due to the preventive action of the salicyl compounds. All that we can do is to satisfy ourselves, first, as to the mode in which the heart complications are brought about; and, second, as to the manner in which the salicyl compounds act. Having done this, we are in a position to judge as to whether or not they are likely to possess any prophylactic properties.

It has been abundantly proved that the salicyl compounds do possess the power of arresting and cutting short the course of rheumatic fever. This means that they possess the power, not only to allay the inflammation which already exists, but also to prevent that which would certainly arise, either in those joints which have already been affected, or in others, if the attack were prolonged. If we admit their power to prevent rheumatic inflammation of the joints, we must also admit their power to prevent similar inflammation of the heart.

If the view which has been advanced as to their mode of action be correct, they cannot fail to prevent cardiac complications, *if only they are given in sufficient quantity to destroy the rheumatic poison before this has begun to affect the heart.*

The chief obstacle to their doing so, is the early stage at which the hear is apt to suffer. It is only in a minority of cases that time and opportunity are given to get the full action of the salicyl compounds, before the heart is affected. This is specially the cases in hospital practice, in which the patients seldom come under notice before the disease has existed for the best part of a week.

The very acute cases which come under observation during the first two or three days of the illness, are also the ones in which the heart is apt to be affected from the commencement. In such cases, the joint and heart affection are often contemporaneous; though, for reasons already given, the symptoms of the latter are more slowly developed.

In subacute cases, the symptoms are developed less rapidly, and the heart affection is more likely to be delayed a few days; but so also is the period at which treatment commences, for such cases are generally ailing for at least three or four days before they come under notice.

In acute cases, the heart affection is developed so soon, and so quickly, that there is no time to get the prophylactic action of the salicyl compounds. Subacute cases come under notice at so comparatively late a period, that there is no opportunity to do so.

So that, whatever prophylactic properties we may accord to the salicyl compounds on theoretic grounds, there remains the difficulty that in actual practice this result is seldom attainable. All that we can say is, that it may be got in some cases; but in no given case can we be sure of having got it.

With such a possibility before us, however; and with such a tremendous issue at stake, it is impossible to exaggerate the importance of the early and free administration of the salicyl compounds in all cases of acute and subacute rheumatism; for we never know when we may be dealing with a case in which prophylaxis is attainable. The bare possibility of such a result is worth striving for. But promptitude and decision are requisite to success. A halting spirit, and inadequate dose, court failure. At least thirty grains should be given every hour till there is decided evidence of action, and then the dose should be

diminished slowly. A delay of a few hours in commencing treatment, or the administration of the drug in insufficient dose, may make all the difference between perfect recovery and recovery with a damaged heart—a calamity which, in some cases, is scarcely preferable to death, so hard may be the conditions under which life is carried on.

Do the salicyl compounds have a curative action in rheumatic inflammation of the heart?

Regarding such inflammation as identical in nature and pathology with rheumatic inflammation of the joints; and recognizing the distinctly curative effect of the salicyl compounds in the latter, it might, not without reason, be expected that they should have the same action in the former—that they should cure rheumatic carditis, as they do rheumatic arthritis. Experience, however, has shown that such is not the case; and that under the salicyl treatment, as under all others, rheumatic endocarditis (to which we shall still confine our attention) generally, if not always, leads to permanent damage.

Attention has already been drawn to one obstacle which intervenes to make the treatment and cure of inflammation of the heart specially difficult—the impossibility of giving rest to the inflamed textures. This is an obstacle which no treatment can overcome. It is an important factor in keeping up the mischief originated by the rheumatic poison, and affords an adequate explanation of the fact, that the treatment which allays acute rheumatic inflammation of a joint, may fail to have a like action in similar inflammation of the heart. In both, rest is essential to quick recovery. In the one it is easily obtained; in the other it is unattainable.

But it is not enough to explain why the ailment should be so little amenable to treatment during its acute stage. We have also to account for the permanent duration of the endocardial mischief.

Pericarditis may be perfectly recovered from, the effused products may be absorbed, and the membrane restored to its natural state. So, too, may myocarditis. But we cannot say the same of endocarditis. Its signs persist after all inflammatory mischief has ceased. It is a pathological fact, that when once a certain amount of change has taken place on the endocardial surface, the damage is irremediable and permanent. The endocardium is the only structure habitually affected

by the rheumatic poison, of which this can be said. The fact demands, and admits of, explanation.

The endocardium is the only structure in the heart which has no analogue, anatomical or physiological, in the joints. The fibrous and muscular textures of the heart and joints have a like structure and function. So have the pericardial and synovial membranes. The endocardium alone is unrepresented in the loco-motor apparatus. It stands alone, too, in its pathology. Its scanty vascularity, and low vital activity, make it insusceptible to acute general inflammation; such inflammation is, therefore, unknown in connection with it.

The same circumstances also intervene to prevent the absorption of products effused on its valvular portion during an attack of rheumatic endocarditis. To the absorption of such products a certain degree of vascularity is necessary: such vascularity does not exist in the endocardium; and, therefore, lymph deposited on its surface is not absorbed.

It may, indeed, be said that a degree of vascularity which suffices for the effusion of lymph, should suffice also for its absorption. But the lymph deposited on the valves during rheumatic endocarditis is not all effused. Great part of it is deposited directly from the blood, on the roughened surface; and even this primary roughening results from irritation caused, not directly by the rheumatic poison, but by friction of the valvular surfaces, produced in the manner already explained—a mechanical force which, in the case of the heart, cannot be equalled or counterbalanced by any agency which stimulates absorption. The only force which could have this effect is occasional pressure; and that is not available.

It is evident that the condition is one on which medicinal treatment can have no effect; and thus is explained the inability of the salicyl compounds to repair the damage done during an attack of rheumatic endocarditis.

The direct cause of all the objective, and most of the subjective, symptoms of endocarditis, is not the rheumatic poison which causes the inflammation—it is not even the inflammation itself,—it is the physical change caused by the rubbing and roughening of the swollen valves. The lymph deposited during rheumatic inflammation of the heart, differs in no respect from that thrown out during non-rheumatic

inflammation. No one would expect the salicyl compounds to remove the latter. It would be as unreasonable to expect them to remove the former. These drugs are not deobstruent, they are anti-rheumatic. They cure rheumatic fever; but they do not stimulate absorbents, or remove effused products.

The fact that the salicyl compounds are powerless to remove cardiac damage, is an urgent reason for getting the system under their influence and out of that of the rheumatic poison, before the heart becomes involved.

But though they fail to effect a cure, it cannot be said that these compounds are totally without influence in cardiac inflammation. For if their action on the rheumatic poison be such as we suppose, they cannot fail to be of some benefit. If they destroy the rheumatic poison, they must, by so doing, curtail the duration, and limit the extent, of its action on the heart, and so mitigate the severity of the cardiac mischief.

It is, of course, impossible to demonstrate, in any given case, that the heart inflammation has been allayed by the treatment; for the disease does not tend to death in more than a minority of cases. But it is equally impossible not to see that, in some cases, the salicyl treatment must tend to mitigate the severity of the heart inflammation, and to some extent allay the cardiac disturbance. The following case will serve to illustrate this. It is the same patient as Case VI., already given. It was formerly instanced as evidence of the beneficial action of salicin in the joint inflammation; it is now given in illustration of its action in rheumatic inflammation of the heart.

A previously healthy girl, aged sixteen, was seen on the third day of a severe attack of acute rheumatism. She was in bed, unable to move, and actually screaming from the violence of the joint pains. The back, shoulders, elbows, wrists, knees and ankles were all the seat of severe pain; and the joints were so exquisitely tender that the least touch or movement of the bed caused her to scream with agony. The skin was hot, not perspiring; the tongue moist and furred; the urine scanty, high colored, and loaded with pink urates. The pulse was 112; respirations 20; the temperature 103.8°. There was no pain or uneasiness in the chest; but there was a soft blowing murmur with the

first sound, loudest at the apex, but audible over the whole heart. She had fifteen grains of salicin every hour for three hours, and then fifteen grains every two hours.

She wandered a little during the night, but had occasional snatches of sleep.

On the following day (the 17th April), after 120 grains of salicin had been taken, she felt much better, though still in pain; she could move the right leg a little, and allowed the joints to be pretty firmly grasped without complaining. On the previous day the least touch made her scream. The skin was covered with acid perspiration. The pulse was 96; respirations 26; temperature 102.8°. The cardiac blow was softer in character, and preceded as well as accompanied the first sound at apex; it was less distinct over body of heart.

On the 18th, after 270 grains of salicin had been taken, she felt quite well; had no pain, and could move the limbs freely without any other sensation than some degree of stiffness of the joints. The pulse was 72, very feeble; respirations 20; temperature 99.6. The heart's action was irregular; the murmur had lost its systolic character, and was now short and purely præsystolic, distinct at apex, but not audible an inch from it.

On the 19th, after having had 405 grains of salicin, the pulse was 70, the respirations 20, and the temperature 98.2°. The girl felt perfectly well. She had no subjective symptom of heart disease, but the præsystolic murmur remained, and there was some irregularity of the heart's action.

This was a very severe attack of acute rheumatism. When first seen, on the third day of her illness, the heart and all the large joints were the seat of acute inflammation, she was screaming with agony, and the temperature was 103.8°, more than five degrees above the normal. Within forty-eight hours, she felt quite well, was entirely free from pain, and the temperature had fallen more than four degrees.

That the salicin cured the joint affection there can be no doubt. It did so by destroying the rheumatic poison. For reasons already given, it could not exercise the same curative effect on the heart inflammation. But that it served to mitigate its severity there can be no reasonable doubt. Indeed, a careful consideration of the matter tends to show that such could not fail to be its action. For if it destroyed the

rheumatic poison, it must almost certainly have had a beneficial effect on the inflammation to which that poison gave rise in the heart.

But this is not the only way in which it tended to mitigate the severity of the heart affection. Under its influence the joint inflammation subsided, and the febrile disturbance came speedily to an end. This result was accompanied by greatly diminished frequency of the heart's action. As a matter of fact, the cardiac pulsations fell in thirty-six hours from 112 to 72—a fall of 40 a minute, 2400 an hour, or 57,600 a day. It is needless to point out, that this diminished frequency of the heart's action implied decreased functional activity of the inflamed textures; and that such decreased functional activity is the one condition which is most desired, and most difficult to attain, in the treatment of cardiac inflammation.

Had the rheumatic process not been cut short by the salicin, the rheumatic poison would probably have continued to act for some weeks; the pulse would have continued to beat at the rate of 112 per minute, if not more; the inflamed valves would have been every day subjected to the strain involved in their action 57,600 times more frequently than was the case. At the end of a week they would have been strained 1,128,960 times, instead of only 725,760; that is, 403,200 times more frequently—an enormous difference, which could not fail to tell on the morbid process.

It is evident from this, that independently of the good which may have resulted from the destruction of the rheumatic poison, benefit must have accrued to the heart from the diminished frequency of its action, consequent on the arrest of the joint inflammation and accompanying fever.

The disappearance of the systolic blow when the system was brought under the influence of the salicin, is a noteworthy fact. It may have been brought about in one of two ways: either the morbid change which gave rise to it was removed; or there was so small a quantity of lymph effused that the quieting of the heart's action, by permitting of the more deliberate closure of the valves, led to less strain, less forcible closure and contact of the segments, and so to diminution of friction, and consequent repair. The continuance of the præsystolic blow would seem to indicate that the latter was the true reason for its disappearance. Whichever view we adopt, the fact remains that the

systolic blow disappeared about the time that the anti-rheumatic effect of the salicin was got. So rare is the disappearance of such a sign, that one cannot fail to see a possible connection between it and the coincident decline of the joint inflammation; and to connect both with the action of the salicin.

Had the rheumatic symptoms continued, and had the heart gone on beating at the rate of 112 per minute, it is in the highest degree probable that the damage to the valve would have increased, that the surface would have become more roughened, that the blood would have continued to regurgitate into the auricle, and that this condition would have been permanent. From this disastrous result the girl was probably saved by the salicin.

The general conclusion to which we have come is, that the early and free administration of the salicyl compounds holds out the best chance, both of saving the heart from the action of the rheumatic poison, and of mitigating the severity of that action, when it is too late to prevent it; but that these compounds are powerless to remove effused products, after the heart mischief is fully established.

The general treatment applicable to rheumatic inflammation of the heart, is thus the same as that which is applicable to similar inflammation of the joints. The existence of heart complication in a case of acute rheumatism, is not only no reason for omitting the salicyl compounds, but is an additional one for giving them freely, and in large dose.

In the great majority of cases no other treatment is required. But every now and then a case occurs in which considerable benefit is got from the adoption of local measures.

In pericarditis especially, local treatment is sometimes of much importance. In the early stage of a severe attack, when pain is a prominent symptom, when the heart's action is disturbed and tumultuous, and when there is evidence of serious interference with the circulation, much good may be got by abstracting a few ounces of blood. This may be done by opening a vein, or by the application of leeches, or cupping glasses, over the region of the heart. If the symptoms are urgent, venesection affords the most speedy relief; but to do good, it must be had recourse to at an early stage. The cases are few, however, in which the desired effect may not be got from leeches.

In entertaining the question of bleeding, local or general, it must be borne in mind that the acute stage, when got over, is followed by one in which there is apt to be considerable depression and debility. If bleeding be had recourse to unnecessarily, or too freely, this stage will be rendered more marked and prolonged. The mere existence of acute pericarditis is not a reason for taking blood; such a measure is to be regarded only as the best means of allaying the urgent symptoms of the first stage of a very acute attack.

Cold, as got by the application of an ice-bag over the region of the heart, may be of benefit at this stage. It is to be prescribed only during the acute stage. In milder cases warm poultices often give relief.

After the acute stage has been subdued there is generally, especially in severe cases which have required active treatment, some effusion of fluid into the pericardium. In most cases this disappears as convalescence advances and strength returns. But occasionally it is necessary to adopt measures for its removal.

Blisters repeatedly applied over the heart, and the internal administration of deobstruents, such as mercury and iodide of potassium, are the remedies usually recommended. Blisters are certainly of use; but the debilitated condition of the patient, and the weakened state of the cardiac muscles, which suffer more or less in acute cases, indicate the use of good food and tonics.

If these measures fail, and especially if the quantity of fluid be so great as to cause serious inconvenience, it may be necessary to have recourse to tapping. The trocar of an aspirator may be introduced into the distended sac without difficulty. The best point for its insertion is the fifth intercostal space, to the left of the sternum, care being taken to avoid the line of the internal mammary artery. Whether or not the operation may be ultimately successful, it always affords relief for the time. But the operation is one which is rarely called for.

In endocarditis it is very questionable if local measures ever do good. If the case is very acute, and accompanied by evidence of distress, a few leeches may be applied. But all depletory measures should be used with extreme caution. So, too, they should in myocarditis.

There is no especial treatment applicable to myocarditis: it is

essentially symptomatic. But, as a rule, the treatment of the acute stage is the same as that of endocarditis. When that stage passes off, the administration of tonics is called for.

Attention has already been drawn to the change in the cardiac walls induced by inflammation. They become abnormally soft and weak. It is at all times of importance that the occurrence of such a change should be recognised. It is specially so in connection with the salicyl treatment.

When considering the respective merits of salicin and salicylic acid, we saw that the latter had for one of its drawbacks a depressing action on the heart, evidenced by feebleness and, generally, increased rapidity of its action; and one or two cases were instanced to show, not only that salicylic acid produced this effect, but that no such inconvenience attended the use of salicin.

In the treatment of the heart complications of acute rheumatism, it is of importance that this action of salicylic acid should be borne in mind. If there is any reason to suspect the existence of inflammatory softening of the walls of the heart, salicylic acid, if given at all, should have its action on the heart watched very narrowly. If there is any evidence of the existence of myocarditis, or of feeble cardiac action, it should not be given at all; for the addition to the already existing enfeeblement, of such depression as salicylic acid may cause, might add seriously to the patient's danger. It is not in every case that salicylic acid has an enfeebling action on the heart; but one never knows when such a case may occur. To give a remedy which may have such an action, in an ailment in which cardiac enfeeblement is the special danger with which we have to deal, is a practice which one cannot but condemn, for it cannot fail at times to produce injurious results. Fortunately it is a practice which is never called for, even in the interests of the joints; for we have in salicin a remedy which, as an anti-rheumatic, is as potent as salicylic acid; and which possesses over that acid the enormous advantage of having no depressing action on the heart.

In all cases of recent inflammation of the heart, the muscular substance is liable to be affected. In all cases in which it is affected there is produced a soft and enfeebled condition of the ventricular walls. In

all such cases the administration of salicylic acid is attended with appreciable risk.

Rest, quiet, good food, tonics, and stimulants in moderate quantity, are the remedial agencies to which we must trust in the treatment of this softened condition of the heart's walls.

The ailment is one which nearly always occurs in young people; at an age, that is, at which the system possesses great recuperative powers. If not fatal in the acute stage, recovery is generally perfect. Attention has already been drawn to the fact that it may cause sudden death. The risk of such an accident would be increased by the depressing action of salicylic acid.

CHAPTER XVIII.

CEREBRAL RHEUMATISM.

It was at one time believed that head symptoms occurring in the course of acute rheumatism were symptomatic of inflammation of the membranes of the brain. This inflammation was looked upon as due to metastasis—to a retrocession of the rheumatic disturbance from the joints to the brain. And there are on record one or two cases in which there was found, after death, distinct evidence of inflammatory change in the cerebral membranes.

But as observations increased, and *post-mortem* evidence accumulated, it was found that, in the majority of cases of acute rheumatism which proved fatal apparently by head symptoms, the brain and its membranes were normal in appearance, and gave no evidence of inflammatory disturbance.

In several cases in which these symptoms were prominent, and in which the fatal result was attributed to intra-cranial mischief, the only evidence of inflammation was found in the heart and pericardium. From this the conclusion was drawn, that cerebral disturbance occurring in acute rheumatism, was symptomatic of inflammation about the heart. This conclusion, though quite accurate in some cases, is not applicable to all; for there have been recorded not a few fatal cases of acute rheumatism, in which the head symptoms were marked during life, but in which no *post-mortem* evidence of inflammatory mischief could be found in heart, brain, or any internal organ. Of late years, clinical observation, though it cannot be said to have much advanced our knowledge of the pathology of these cases, has thrown considerable light on their symptomatology. The introduction of the thermometer, as a means of clinical research, has shown that some cases of acute rheumatism which are characterized by the occurrence of head symptoms, rapid failure of strength, and a speedily fatal termination, have also for one of their most striking peculiarities, a rapid and great rise of temperature. Instead of ranging from 101° to 103° or 104°, it

rapidly runs up to 106°, 108°, 110°, or even more. So characteristic is this range in connection with such symptoms, that the condition is now generally referred to as one of "rheumatic hyperpyrexia."

Head symptoms thus occur in acute rheumatism under three different conditions:—

1. As a symptom of inflammation of the membranes of the brain.

2. As a symptom of inflammation of the substance, or membranes, of the heart.

3. In connection with very high temperature of the body.

We shall consider each separately.

1. Rheumatic Meningitis.

There are recorded a few cases of acute rheumatism, in which the occurrence of marked head symptoms during life, and the presence of lymph, and even pus, on the surface of the brain after death, show that meningeal inflammation may occur in the course of that disease. But meningitis, occurring in the course of acute rheumatism, is not necessarily of rheumatic origin. The extreme rarity of such cases, indeed, suggests a grave doubt whether, in the few cases in which it did occur, the meningeal mischief was not an accidental complication, due to the action of some other agency than the rheumatic poison. Certain it is, that the very small proportion of cases in which such a complication occurs, detracts from the interest and importance which would otherwise attach to it; and leads to the practical conclusion that, of all possible causes of head symptoms occurring in the course of acute rheumatism, inflammation of the membranes of the brain is the least likely to be the one with which, in a given case, we have to deal.

The symptoms to which such inflammation would give rise, would not differ from those of similar inflammation occurring independently of rheumatism. Its treatment, too, would be the same, except that appropriate anti-rheumatic remedies would be conjoined with the measures specially suited to the local head affection.

2. The Nervous Symptoms of Carditis.

To the occurrence of head symptoms in connection with inflammation of the heart and its membranes, attention has already been directed, and two cases (Cases I. and II.) have been given in which all the symp-

toms during life pointed to inflammatory mischief within the cranium, but in which, after death, there was found nothing abnormal within the head, but only the indications of inflammation of the heart and its investing membrane. Since these cases were recorded, much attention has been given to this subject, and the observations of Bouillaud,[1] Macleod,[2] Hawkins,[3] Bright,[4] Burrows,[5] Latham,[6] Fuller,[7] Watson,[8] and others, have demonstrated that inflammation of the heart and its membranes, is a frequent cause of head symptoms in acute rheumatism.

It is chiefly in connection with pericarditis that they have been noted. This is probably due to its greater frequency, and more easy diagnosis, as compared with myocarditis. In simple endocarditis, head symptoms are rarely noted.

But symptoms directly referable to the brain, such as delirium and coma are not the only nervous symptoms which may occur in connection with cardiac inflammation. Sir George Burrows[9] states that "there is scarcely an affection of the cerebro-spinal system which may not be simulated by inflammatory disease of the heart and its membranes." He gives five different classes of cases: "(1) cases which were marked with all the usual symptoms of inflammation of the brain and its membranes; (2) cases simulating mania and dementia; (3) cases characterized by apoplectic and epileptic symptoms; (4) cases with well-marked symptoms of tetanus and trismus; and (5) others still more numerous, accompanied by symptoms of aggravated chorea and hysteria."

How are these symptoms to be accounted for? Nervous symptoms occurring in connection with inflammation of the brain admit of easy explanation. It is otherwise with those occurring in connection with inflammation of the heart and its membranes.

---

[1] Bouillaud, Traité sur les Maladies du Cœur.
[2] Macleod, On Rheumatism.
[3] Hawkins, Lectures on Rheumatism.
[4] Bright, Medico-Chirurgical Transactions, Vol. XXII.
[5] Burrows, On Disorders of the Cerebral Circulation.
[6] Latham, Lectures on Diseases of the Heart.
[7] Fuller, On Rheumatism.
[8] Watson, Practice of Medicine.
[9] Burrows, op. cit., p. 185.

Various hypotheses have been advanced as to their mode of production.

1. They have been attributed to a vitiated state of the blood. "A distempered condition of the blood I conceive to be the true proximate cause of the sensorial disturbance occasionally observed in the course of acute rheumatism," says Fuller.[1] "Those remarkable cerebral affections—the wild delirium aud violent mania—which not unfrequently occur in the course of rheumatic fever, or follow in its train, and which have usually manifested themselves along with the cardiac complication, causing doubt and perplexity in the mind of the physician as to the real organ affected, and the true nature of the disease, are to be explained by the morbid condition of the blood which is admitted to exist in the rheumatic constitution." So wrote Begbie,[2] the distinguished father of him to whose memory this book is dedicated.

But if this morbid condition of the blood sufficed for their production, such nervous symptoms would be common in rheumatic fever. Instead of occurring only in rare and exceptional cases, they would be the rule; and delirium would be as characteristic a feature of rheumatic, as it is of typhus fever.

2. They have been ascribed by some to the action of the rheumatic poison on the cerebro-spinal membranes. But if that were their mode of production, we should find in fatal cases *post-mortem* evidence of such an action. The local effects of the action of the rheumatic poison, as they present themselves in acute rheumatism (and it is only in the acute form of the disease that such nervous symptoms as we are considering occur), are essentially inflammatory; and we recognize no other direct effects in connection with its action. If the nervous symptoms resulted from the action of the rheumatic poison on the nervous centres, we should have evidence of inflammatory disturbance at the seat of its action. But the absence of such evidence is the special peculiarity of the cases which we are now considering. We cannot, therefore, look to the *direct* action of the rheumatic poison for the explanation of their nervous symptoms.

3. By others they have been attributed to metastasis—to a retroces-

---

[1] Fuller, op. cit., p. 289.

[2] Contribution to Practical Medicine, by James Begbie, M.D., F.R.S.E., p. 85. 1862.

sion of rheumatic inflammation from the joints to the nervous centres. But the results of metastatic, would not differ from those of non-metastatic, inflammation; for, so far as its local effects are concerned, it would not matter whether inflammation went to the nervous centres from the joints, or originated in them independently of any prior joint affection. As it is the absence of local inflammation in the nervous centres that constitutes the peculiarity of these cases, it is evident that we cannot look to metastasis for the explanation of their peculiar symptoms.

Bouillaud thought that nervous symptoms were most apt to occur in cases of pericarditis which were complicated with pleuritis, and especially in those in which the diaphragmatic portion of the pleura was affected.

Dr. Bright, in discussing the inter-relationship of rheumatism and chorea, expressed the opinion that though the cerebro-spinal coverings were sometimes implicated, "yet the much more frequent cause of chorea in conjunction with rheumatism is inflammation of the pericardium. The irritation is probably conveyed thence to the spine; just as the irritation of other parts, as of the bowels, the gums, or the uterus, is communicated, and produces the same diseases." He further made the definite suggestion that the phrenic nerve was the "immediate means of communicating the irritation to the spinal cord."

The similarity between the views of Bouillaud and of Bright is apparent. But though their explanation might apply to some cases, it cannot be accepted for all. For, as pointed out by Burrows, rheumatic pericarditis may be complicated with pleurisy, without giving rise to nervous symptoms; and such symptoms may be marked in cases of pericarditis in which there is no affection of the pleura. In one of the most acute cases of rheumatic pericarditis which I ever saw, occurring in a previously healthy and robust woman, twenty-seven years of age; and in which, after death, both layers of the pericardium, and the whole diaphragmatic and corresponding pulmonic surface of the left pleura, were found covered with recently effused lymph, there were during life no nervous symptoms, but only those of cardiac and pulmonary embarrassment.

4. Recognizing the insufficiency of the above hypotheses to account

for the nervous phenomena with which we are dealing, Sir Thomas Watson[1] thought they might be due to disturbance of the cerebral circulation, resulting from embarrassment of the heart's action. The objections to this view are (1) that the delirium may be violent from the very commencement, and before there is any evidence of heart affection; and (2) that the cases in which nervous symptoms are most marked, are not, as a rule, those in which evidence of cardiac embarrassment occurs; but, on the contrary, those in which there are no subjective symptoms of heart disturbance, and nothing to direct special attention to that organ. Moreover, similar nervous symptoms may occur in connection with inflammation of the lung or pleura, without any inflammation of the heart or its membranes.

Clouston was inclined to attribute the symptoms in two cases of "rheumatic insanity" to rheumatic inflammation of the connective tissue of the cerebro-spinal centres. But he brings forward no pathological evidence in support of this view.

Such are the various hypotheses.

In discussing the pathology of nervous symptoms occurring in connection with rheumatism, it seems to me that error has arisen from not sufficiently discriminating between their various forms; and from regarding all nervous symptoms, no matter how different, as having a like causation. The alarming and the trivial have been slumped together, and one narrow pathological view advanced for their common explanation.

It is surely unreasonable to regard such alarming head symptoms as those noted in Cases I. and II., occurring in the course of such a formidable disease as acute inflammation of the heart, as due to the operation of the same cause, and produced in the same way, as the comparatively trivial muscular twitchings noted in cases of rheumatic chorea. And yet that is what has been done.

This manifest source of error we shall avoid by according to each a separate consideration.

The subject of rheumatic chorea we shall take up after we have discussed the pathology of the nervous symptoms now before us—those

---

[1] Watson, Practice of Medicine.

[2] Journal of Mental Science, July, 1870.

noted in connection with acute inflammation of the heart and pericardium.

In studying the pathology, and mode of production, of these symptoms, three possible causes have to be considered:—

1. The morbid condition of the blood, characteristic of rheumatism.

2. The cardiac inflammation.

3. The nervous constitution of the patient.

Hitherto, attention has been directed to the first two; and but little heed paid to the third. This third seems to me to be the most important factor of all.

It is only in exceptional cases of pericarditis that nervous symptoms occur. An exceptional symptom results from an exceptional cause, and calls for an exceptional explanation. The rheumatic constitution, and the inflammation, operate in every case of rheumatic pericarditis. Of the three possible factors, the nervous constitution of the individual is the only one which can be exceptional. It is, therefore, the one which is most likely to give rise to exceptional symptoms.

In all acute febrile ailments, nervous symptoms are apt to occur. Those in whom they are most likely to declare themselves, are persons of susceptible and delicate nervous organization. They are, therefore, more common in women than in men; in young people than in those of more mature years, and in those who have already suffered from nervous disturbance than in those who have not so suffered.

Now, in looking over the recorded cases in which nervous symptoms have occurred in connection with pericarditis, it is found that they have nearly all occurred in women and boys, and that the few adult males who thus suffered had already been the victims of some abnormal condition of the nervous system. Of the sixteen cases collected by Burrows, for instance, nine occurred in females, and seven in males; but of the males, only two were over twenty-one years of age; and of these two one was a man of intemperate habits, and the other "suffered from asthma, sleepless nights, cough and expectoration, and at the same time from spasmodic contractions of the muscles of the extremities." What determined the prominence of the nervous symptoms in these cases, was not the rheumatic constitution, and not the

inflammatory nature of the case, but the special susceptibility of the nervous systems of those in whom that inflammation occurred.

In his remarks on Case I., already quoted, Andral says, "Qu'en raison des susceptibilités individuelles, il n'est point d'organ dont la lésion ne puisse déterminer les symptômes nerveux les plus variés, de maniére à produire sympathetiquement les différens états morbides dont on place le siége dans les centres nerveux et leurs dépendances."

It is this individual susceptibility that forms the important feature of the cases whose peculiar symptoms we are endeavoring to explain, and it is the non-recognition of this factor that makes the explanations hitherto given of these symptoms, so unsatisfactory and inadequate.

Head symptoms occurring in connection with acute myocarditis and pericarditis, we regard as exceptional, as indicative of an unusually susceptible nervous system, rather than of any peculiarity of the disease, and as owning a pathology, and mode of production, differing in no material respect from those of like symptoms as they occasionally occur in connection with pneumonia, pleurisy, and other acute inflammatory disorders.

But though thus insisting on the importance of constitutional susceptibility as a predisposing and determining cause, due importance must also be attached to that which is to be regarded as the direct exciting cause of the disturbance—the inflammation; and there is probably some truth in the statement of Bouillaud, that the more extensive the local inflammation, the more likely is the nervous system to be affected.

From what has been said, it will be seen that the rheumatic aspect of the case is not regarded as of importance. I do not think that it has much to do with the production of the symptoms which we have been considering, the head symptoms which occur in some cases of myocarditis and pericarditis.

It is the acute inflammation of the heart, or of its investing membrane, that is to be looked to as the exciting cause of the disturbance. Such inflammation rarely occurs except in connection with rheumatic fever, and hence, such nervous symptoms as accompany it are equally rare except in connection with that disease. That it is with the in-

flammation, and not with the rheumatism, that they have a causal connection, is evidenced by the fact that they do occur in the rarer non-rheumatic, as well as in the more common rheumatic, forms of cardiac inflammation. "Of the sixteen cases I have narrated," says Burrows, "no rheumatic affection could be discovered in seven of them."

CHAPTER XIX.

THE RELATION OF RHEUMATISM AND CHOREA.

Of the existence of some relation between rheumatism and chorea, there can be no doubt. The observations of Bright,[1] Begbie,[2] Hughes,[3] Burton Brown,[4] Sée,[5] Roger,[6] and others, have placed this beyond doubt. Their evidence need not be reproduced here.

What we have to do, is to consider the nature of this relation, and the bearing of the rheumatic constitution on the choreic symptoms. It is necessary to do so, for no theory of rheumatism can be regarded as satisfactory which does not recognize, and at least coincide with, this relationship; and no view of the nature of the rheumatic constitution can be accepted as valid which does not consist with its existence.

Chorea is essentially a disease of the nervous system. Its characteristic symptom is irregular and uncontrollable muscular twitching and jerking.

For the explanation of such a symptom we turn, not to that part of the nervous centres whose derangement causes delirium, wandering, and such phenomena as were noted in connection with inflammation of the heart, but to that part of them whose function it is to initiate, control, and regulate movement—the motor centres. How the rheumatic constitution leads to disturbance of these centres, is the question which we have to solve.

There are two views on this point: one that the choreic symptoms result directly from the disturbing action on the nervous centres of the vitiated blood; the other that they are directly due to a prior affection of the heart—the rheumatic condition acting only indirectly through this.

---

[1] Medico-Chirurgical Transactions, Vol. XXII.
[2] Begbie, op. cit.
[3] Hughes, Guy's Hospital Reports, 1846.
[4] Burton Brown, Guy's Hospital Reports, 1856.
[5] Mémoires de l'Académie de Médecine, Vol. XV., 1850.
[6] Archives Générales, Vol. II., 1866, and Vol. I., 1867.

The former view is that advocated by Begbie. "I cannot help coming to the conclusion that the simple and true view of the relation of rheumatism and chorea is to be found in the morbid condition of the blood, which is admitted to exist in the rheumatic constitution, and this explanation will apply equally to chorea occurring in individuals or families inheriting the rheumatic diathesis; to chorea occurring in connection with rheumatism, but without the cardiac complication, and to chorea associated with pericarditis, or endocarditis, or both—the inflammatory affections of the fibrous tissues, as well as the spasmodic affection of the muscles, and the derangement of the nervous system, originating in the same specific disorder of the circulating fluids."[1] To this explanation of the choreic symptoms, there is the same objection that applied to a like mode of accounting for the nervous symptoms noted in pericarditis. If due to the morbid condition of the blood, they ought to be much more common than they are, for that is a cause which operates in every case of rheumatism. Occurring, as they do, only in exceptional cases, they are more likely to result from an exceptional cause, than from one which operates so generally.

The view that the chorea is consequent on a prior inflammation of the membranes of the heart, is that which has commended itself to most other observers. There is some variety of opinion, however, as to the sequence of events by which the one phenomenon leads to the other.

Reference has already been made to the opinion of Bright, that the choreic symptoms resulted from irritation transmitted from an inflamed pericardium or pleura along the phrenic nerve. This explanation might apply to cases of chorea occurring in connection with pericarditis or pleuritis, but is quite inapplicable to the numerous cases in which no such inflammation exists.

In more recent times the view has been advanced and ably advocated by Kirkes, Hughlings Jackson, Broadbent, and others, that it is to endocarditis rather than to pericarditis that we have to look for the explanation of the choreic phenomena. The theory is, that some of the particles of lymph, effused on the surface of the valves, get detached, enter the circulation, and cause embolic plugging of the minute

---

[1] Begbie, op. cit., p. 84.

vessels of the motor ganglia, and some pathological evidence has been adduced to show that the corpora striata and optic thalami have suffered in fatal cases of chorea. The actual existence of embolism, however, has not been demonstrated, and its occurrence, as a cause of chorea, cannot be regarded as more than hypothetical. That such an event is possible, there can be no doubt; but if particles of fibrine are detached from the valvular surface, it is difficult to see why the vessels of other parts of the brain should not be plugged, as well as those of the motor ganglia, and why these embolic particles should not sometimes get into other organs, and give rise to infarctions of the lung, spleen, kidney, etc.

Again, if the cause of chorea in rheumatic subjects be the detachment of particles of lymph from the surface of a roughened valve, how are we to explain its occurrence in those numerous rheumatic subjects whose valves have never been affected? To such cases this embolic theory is quite inapplicable. It cannot, therefore, be regarded as adequate. Just as Bright's theory might apply to cases of chorea occurring in connection with pericarditis, so this one might apply to cases of chorea occurring in connection with endocarditis. The fault of each is its narrowness, and the impossibility of applying it to more than a minority of the total cases of rheumatic chorea. What we want is an explanation which will apply to all cases of that disease—those occurring in connection with pericarditis—those occurring in connection with endocarditis—those occurring in connection with simple rheumatism of the joints, uncomplicated by any heart affection—and those occurring in persons of rheumatic constitution, but who, at the time of the choreic attack, are not suffering from rheumatism of either the heart or joints.

The theories hitherto advanced have given prominence to two different factors—the morbid condition of the blood, and the inflamed condition of the heart. Neither has been sufficient to meet the whole of the facts. A much wider pathological view is required for that purpose. Such a view we have in the theory advanced in these pages as to the nature of rheumatism.

Rheumatism is essentially a disease of the motor apparatus: chorea is essentially a disease of the motor centres.

In this broad pathological statement we have the clue to the explanation of the relation of the two diseases.

The motor centres affected in chorea, and the motor apparatus which suffers in rheumatism, have an essential physiological connection. The motor centres form the central portion of a system, of which the motor apparatus is the distal or peripheral. Each is essential to the physiological completeness of the other, and without the other, neither has any physiological *raison d'être*. Without joints to be moved the motor centres would be useless: without motor centres to initiate the necessary nervous force, the muscles would remain flaccid, and the joints be of no avail.

The seat of chorea and the seat of rheumatism having so close a physiological connection, it need not surprise us to find that there is some connection between these two diseases, and that those who are subject to the latter, are also liable to have the former.

The existence of the rheumatic diathesis implies a liability to disturbance of the motor apparatus. The motor ganglia are an essential part of this apparatus. Those subject to rheumatism are therefore, *cæteris paribus*, more likely to have susceptible motor centres than those who are not. Thus the rheumatic diathesis predisposes to chorea. So much physiology teaches. But the practical questions still remain—How is the chorea induced? What is its exciting cause? and Why does it occur only in a small percentage of the total number of rheumatic subjects?

Here, as in the case of the nervous symptoms of pericarditis, constitutional predisposition plays an important part. The motor centres, like all other parts of the nervous system, are more susceptible, and more liable to disturbance, in females than in males, and in young people than in those of more mature years. We accordingly find that it is in females and in young people that choreic symptoms are most apt to show themselves. The rheumatic constitution is by no means necessary to their production. A fright, or nervous shock, gastric or uterine derangement, may give rise to chorea and be the exciting cause of the disease in persons in whom there is no history of rheumatism. But many cases there are—so many that the connection is too striking to have escaped detection—in which a present or prior rheumatic attack, with or without heart affection, is the only cause to which the chorea can be traced. Many cases there are, too, in which a rheumatic family history forms the only noteworthy feature.

In discussing the pathology of rheumatic chorea, we thus have two different classes of cases to deal with—those in which the chorea occurs either in connection with, or subsequent to, a rheumatic attack, and those in which there is only a family history of rheumatism.

A rheumatic attack means inflammation of an essential and important part of the motor apparatus, and general disturbance of the whole system. If a nervous shock, or derangement of the digestive or uterine organs, may induce chorea in one predisposed to it, a rheumatic attack may almost certainly do so too, for general rheumatic disturbance of the motor apparatus cannot but be regarded as a possible cause of disturbance of the motor centres. Thus the rheumatic diathesis may be the predisposing, and the rheumatic attack the exciting cause of an attack of chorea. The essential connection of these two causes, and their combination in the same subject, suffice to explain the special tendency of chorea to occur in those who have suffered from rheumatism. The heart complications, to which the choreic phenomena are by some ascribed, are a mere incidental accompaniment of the disease. They may, of course, act as an exciting cause in the same way as the joint affection, but they are not essential to the production of chorea.

But the predisposing cause may exist without the exciting. There may be a family predisposition to rheumatism, without the disease having ever occurred in a given member of the family. With this predisposition there may be combined a special susceptibility of the motor centres, predisposing to chorea; and, for reasons already given, this special susceptibility is more likely to exist in one of rheumatic than in one of non-rheumatic family. Choreic symptoms may show themselves in such a one without any prior rheumatic attack, the exciting cause being some other disturbing agency, possibly one that it may be very difficult to detect, so slight are the causes that may produce disturbance of the nervous centres in young persons predisposed to its occurrence. But no matter what the exciting cause, the disease is fitly described as one of rheumatic chorea, if we recognize that what tended to its production and predisposed to its existence was the rheumatic constitution of the individual.

In a rheumatic subject predisposed to chorea through a susceptible condition of the motor centres, it is an accident whether the chorea,

when it does occur, comes on in connection with a rheumatic attack, subsequently to it, or prior to, and independently of, it. The ultimate pathological explanation of the relation of the rheumatism and the chorea is the same in each; the one disease consists in functional disturbance of the external motor apparatus of the body, the other consists in functional disturbance of its internal motor centres.

CHAPTER XX.

RHEUMATIC HYPERPYREXIA.

In 1867, Dr. Sydney Ringer[1] recorded three cases of rheumatic fever in which, after a week or two of illness, marked only by such symptoms as are common in that disease, there were suddenly developed alarming nervous symptoms; the patients rapidly passed into a state of coma, and speedily died. Coincidently with the onset of these symptoms, there was noted a very remarkable rise in the temperature of the body.

The first case was that of a woman, aged twenty. "She was very delirious during the whole of her illness" (the case was complicated with pericarditis), "and was especially so on the night preceding her death. With the exception of the delirium all her symptoms grew less severe; but she was always very ill. On the morning of the day of her death, she was much worse. She was very restless, and constantly muttered. If her statement could be relied on, she was free from pain. The eyes were bright, and her face flushed, and her breathing much hurried. She continued thus during the day, and at 5 p.m. she was discovered by the nurse to be unconscious. I was sent for at 6.30 p.m., when her breathing was stertorous, and she was profoundly insensible. She died about half an hour after that time. Her temperature was always high. Thus, on the first five days of her stay in hospital it rose to 105°. On the next two days, those immediately preceding her death, it marked only 104°. On the morning of her death, at 9 a.m. it was 105°; at 12, 106.2°; at 3 p.m., 106°; and at, 6, half an hour before her death, 109.2°."

The second case was that of a man, twenty-three years of age, in whom, with the usual symptoms of acute rheumatism, there was evidence of both endo- and peri-cardial mischief, though not to any great extent. "The temperature of his body daily rose to 103.4°, until two days before his death. On the evening before he died it was

---

[1] Medical Times and Gazette, Oct. 5, 1867.

105.4°. At 8 a.m. of the day on which he died it was noticed that he wandered, but this was thought by the nurse to be 'temper.' At 8.30 I was sent for; he was then very delirious; he rolled violently about the bed, and required to be held down. This violence quickly passed away, and he then lay in a half-unconscious state, and moaned loudly. His breathing was irregular and jerking. His eyes were wide open: the pupils were equal and of medium size. The unconsciousness soon deepened, and he could not be roused. He became very pale and rather livid. The lidivity soon greatly increased. His heart, while in this state, beat most violently. His pulse was regular in rhythm and force, and beat 186 in the minute. At 8.40 the temperature of his body was found to be 109.4°; it gradually rose, and at 9.15, the time of his death, it was 110.8°."

The third case was that of a woman, twenty-nine years of age, about whose case there was nothing remarkable till the alarming symptoms came on. "At the time of her admission she suffered from pain in most of her joints; she was always free from pain in the head, and was not delirious till the night before her death. The temperature of her body rose daily to 101° and 102°; but on the evening preceding her decease it reached 104.2°. With the exception of this rise of 2°, up to this time she appeared to be in the same state she had been in on previous days. At about 9 p.m. of this evening she was delirious, and talked much during the night. She got out of bed several times. At 5 a.m. of the following morning she was much quieter. On entering the ward at 9 a.m. I noticed she was very ill; she appeared to be very restless, and rolled her head from side to side; she took no notice of circumstances around; she appeared to be rather delirious, and muttered much; she often contracted her brows and distorted her face with various grimaces; any request that was made of her was instantly obeyed; thus she protruded her tongue when told, etc. Her temperature at this time was 107.8°. At 9.55 it had risen to 108°, and her pulse beat 144 in the minute. Her heart throbbed strongly. At this time her face was flushed, and slightly moistened with perspiration. Her lips, which were dry, had on them some sordes. The pupils were equal and of medium size. Her breathing was irregular, now quick, now slow, always superficial. There was no paralysis of any of her limbs. At 11.20 she was much worse; the insensibility deepened until she

became quite unconscious of pain. Her arms then fell heavily; they occasionally twitched; now it was observed her breathing was stertorous, and that her face had become pale and rather livid. Mucus dried on her eyes; her pulse beat 152 in the minute. 11.38, temperature 109.4°; at this time blood was taken from her arm: 11.55, bleeding discontinued; twelve ounces of blood were withdrawn. She was not in any way benefited by the bleeding; her symptoms and temperature continued the same; and at 12.10 the temperature was 110°. At 1.15 her temperature was 110.8°. At this time she died."

Since the publication of these cases similar ones have been recorded by other observers; and hyperpyrexia has come to be looked upon as one of the most alarming complications of acute rheumatism.

The features common to all the cases are the very high temperature, the prominence of the head symptoms, the tendency to a rapidly fatal termination, and the absence of any *post-mortem* lesion sufficient to account for the alarming symptoms and fatal result.

When death in acute rheumatism is preceded by delirium and coma, one naturally looks to the brain or the heart for an explanation of these symptoms and the fatal termination. But in fatal cases of rheumatic hyperpyrexia there has been found in the brain no lesion, and in the heart only such change as is common in rheumatic fever. In Dr. Ringer's first case "the brain, medulla oblongata, and their membranes were quite healthy." In the second, "the brain and its membranes were healthy, not even congested." In the third, "the brain and its membranes were natural in appearance."

The experience of other observers is the same.

A dark fluid condition of the blood, some congestion of the lungs, and a tendency to rapid decomposition, are the only constant *post-mortem* features. There is nothing in any of these to explain either the symptoms noted during life, or the occurrence of death.

Notwithstanding the absence of local lesion, there can be little doubt that the fatal result in rheumatic hyperpyrexia is due to disturbance of an important part of the nervous centres. The alarming symptoms which precede it, are almost entirely referable to the brain; there is no local complication to explain their occurrence; and death is brought about by coma—by failure of cerebral action.

The questions which suggest themselves for our consideration, are

(1) the mode of production of the high temperature, and (2) the relation which this bears to the brain symptoms and the fatal result.

1. *The mode of production of the high temperature.*

The high temperature of rheumatic hyperpyrexia is due to one of two agencies: either it results from an excess of the same cause which gives rise to the increased heat of ordinary cases; or it results from the operation of an agency peculiar to the cases in which it occurs.

Were hyperpyrexia simply an excess of the ordinary pyrexia of acute rheumatism, and produced in the same way as that, it would occur only in cases marked by unusual prominence of all the symptoms, local as well as general. If the pyrexia of ordinary cases result from the propagation of the rheumatic poison in the system, and coincident inflammation of the fibrous textures; and if the degree of pyrexia be directly as the extent of this propagation and inflammation (as it certainly is); then hyperpyrexia, if simply an exaggeration of the ordinary pyrexia, would be symptomatic of an unusual development of the rheumatic poison, and cases in which it occurs would be characterized by inordinate severity of the rheumatic symptoms. But such is not the case. In those in whom hyperpyrexia has been developed, the disease has, up to the time of its occurrence, presented no peculiar feature. The temperature, the joint pains, the acid sweats, the cardiac complications, the condition of the secretions, have all been such as are daily met with in ordinary cases of rheumatic fever. Prior to the occurrence of hyperpyrexia there has been observed, in the history and course of these cases, nothing to distinguish them from ordinary rheumatic attacks, and nothing to lead one to anticipate the occurrence of so alarming a complication.

Clearly rheumatic hyperpyrexia cannot be regarded as simply an excess of the pyrexia of an ordinary rheumatic attack.

It is an exceptional phenomenon, occurring in only a fractional proportion of the total cases of acute rheumatism. An exceptional occurrence is due to an exceptional cause, and calls for an exceptional explanation. The only exceptional agency which offers itself for our consideration, is some peculiarity of the individual in whom the hyperpyrexia occurs. The question of its causation, therefore, narrows itself into a consideration of the possibility of any individual peculiarity giving rise to such a result.

The temperature of the healthy human body is 98.4°. It is kept up by the heat produced during the various changes, assimilative and disintegrative, which are constantly going on in the tissues.

But if heat-production were constantly going on, without anything to counterbalance it, heat would accumulate in the system, and the temperature would rise above 98.4°. The counterbalancing agency is the heat discharge which is constantly taking place from the pulmonary and cuticular surfaces, chiefly the latter.

Heat is a product of tissue change, just as urea and carbolic acid are; and, like them, requires to be eliminated. The maintenance of an unvarying and equable temperature means the establishment of a proper equilibrium between the heat-producing and heat-eliminating processes. In the healthy body the heat produced varies much from time to time; but increased production is counterbalanced by increased elimination, and the temperature does not rise. During muscular exercise, for instance, there is a great increase in those tissue changes during which heat is formed, but there is not a corresponding rise in the temperature of the body; for the exercise which causes this increased production, is accompanied by a counterbalancing increased frequency of respiration, and increased activity of the skin. There is a feeling of increased heat because of the more active circulation through the skin, but the temperature of the blood is that of health. Just as increased formation of urea leads to increased action of the kidneys, so increased formation of heat gives rise to increased action of the skin, and consequent increased discharge of heat.

But it is extremely unlikely that this delicate equilibrium could be so persistently maintained amidst such constantly occurring changes in heat production and discharge as are inseparable from the daily routine of man's existence, and the widely different and ever-varying conditions of life and climate which he is called upon to face,—it is extremely unlikely that this delicate and finely adjusted counterpoise of production and elimination could, under such circumstances, be so constantly maintained, solely by the crude chemical and physical conditions of tissue change and surface transpiration; or that tissue change and heat discharge should, under all healthy circumstances, be so accurately counterbalanced, that the former could never raise the temperature above, and the latter never make it descend below, the standard of

health. The constancy with which, under the most varied conditions of life and climate, this equilibrium is maintained, points to the existence, besides these purely physical agencies, of some central controlling power, on whose ever-vigilant action the maintenance of this finely adjusted balance is dependent; and which presides over and regulates the production and elimination of heat, just as the motor centres preside over the production, regulation, and proper utilization of muscular movement; and just as the vaso-motor centres control and regulate the distribution of the circulating fluid. Without some such regulating centre, it is difficult to see how the temperature equilibrium could fail to be frequently disturbed by agencies which, as it is, have no effect upon it.

The tendency of modern research is more and more towards the recognition of the doctrine of the localization of cerebral action, according to which circumscribed and limited portions of the brain and cord are believed to preside over, control, and regulate particular acts and functions.

Just as there are centres for the special senses of sight, hearing, taste, etc., so do there exist centres for speech, imitation, mastication, deglutition, etc., whose position in the nervous centres can be defined with more or less exactness. We recognize too, and define the position of, a respiratory centre, a cardiac centre, and a vaso-motor centre.

With the localization of cerebral function thus demonstrated in so many cases; and with the position of various controlling centres more or less accurately circumscribed and defined, we have good *a priori* grounds for regarding the existence of a "thermic centre" as at least probable.

And there is not a little evidence, both physiological and pathological, that such a centre does exist.

The tendency of physiology is towards the recognition of a special set of thermal nerves, distinct from the ordinary nerves of sensation, and having for their function the conveyance to the brain of impressions of heat and cold. When, for instance, I touch any part of the surface of my body with a cold brass button, I feel that the button touches me, and that it is cold. If I touch myself again with the same button slightly warmed, I feel that it touches me as before, but that it is no longer cold. Here there are two distinct impressions: first, that made

on the ordinary nerves of sensation, and by which I know that I am touched; and second, that made on the thermal nerves, by which I know that the button is cold or warm.

If I get into a bath at the temperature of 100°, I feel the water touch me, and know that it is a liquid; but I feel also that it is warmer than a bath of 98° which I may have just got out of, and not so warm as one of 102° into which I may get afterwards. Here there is the same double sensation—that of touch, and that of temperature.

These two sensations are distinct and separate; and one may be felt without the other. I touch the skin of my face with the feathery end of the quill with which I am writing. I feel the touch; but there is no sensation of heat or cold. The nerves of sensation receive the impression: the thermal are not affected by it. I go into a cold room, I allow the fire to go out in that in which I am writing, or I put on thinner clothes than usual, and I feel the change of temperature. I can tell at once whether the temperature of a room is high or low; whether my feet are cold or warm. This knowledge I get through impressions conveyed by the thermal nerves, and without any aid from the nerves of sensation.'

Other evidence in favor of the recognition of special thermal nerves we have in the fact that some parts of the body are more susceptible than others to temperature impressions, without being more susceptible to ordinary touch impressions. If, for instance, I wish to test the heat of a poultice, I do so with the back of the hand rather than with the palm, because I know from experience that the back receives thermal impressions more readily than the palm. But to ordinary touch sensations the palm is more susceptible than the back.

There are other reasons for regarding the existence of special thermal nerves as, at least, not improbable. It is extremely unlikely that the same nerve should be able, at one and the same time, to convey two distinct impressions, or that the same portion of the nervous centres should be capable of simultaneously registering them. The simultaneous conveyance to the brain of two such entirely distinct impressions as those which we have been considering, points to their conveyance by

---

[1] Brown-Séquard thinks there are four different special conductors for (1) touch, (2) tickling, (3) temperature, and (4) pain.

two distinct sets of nerves. The existence of two distinct sets of nerves almost necessarily presupposes two distinct centres—one for each—in which the special impressions of each set of nerves are registered. A belief in the existence of thermal nerves almost necessarily carries with it a belief in the existence of a thermic centre.

That physiology affords reasonable grounds for such a belief, we have just seen.

Pathology, too, points in the same direction.

1. It has been shown by direct experiment that section of the pons at its junction with the medulla oblongata, causes the temperature of an animal to rise.

2. Injuries and diseases of the nervous centres and their membranes, and especially of the cervical portion of the cord, are often accompanied by a very remarkable rise of temperature, for which there exists no reason except the nervous lesion. Since Sir Benjamin Brodie[1] recorded his well-known case, similar ones have been observed by others, in which, after injury to the cervical cord, the temperature of the body rose to 109°, 110°, or 111°. And Mr. Teale[2] has related one in which a patient recovered after the temperature had reached the unprecedented height of 122°.

But in some cases of injury to the cervical cord, the opposite condition is noted; instead of a great rise, there is a great fall of temperature. Mr. Hutchinson[3] has related an instance of crushing of the cord at the level of the fifth cervical vertebra, in which, within twenty-four hour after the injury, the temperature in the urethra was 93°, and in the rectum 95.8°.

3. Pathological records, too, show that when the nervous supply to a given part is arrested by injury or disease, the temperature of the part thus isolated falls below the normal. This fact has been attributed to diminished functional activity of the paralyzed part, and consequent decreased blood supply. But that explanation cannot apply to all cases. "When, for instance, after section of the ulnar nerve, the temperature

---

[1] Medico-Chirurgical Transactions, 1837.

[2] Transactions of Clinical Society of London, 1875.

[3] Clinical Lecture on the Temperature and Circulation after Crushing of the Cervical Spinal Cord, by Jonathan Hutchinson, Senior Surgeon to the London Hospital. (*Lancet*, May 22, 1875.)

at a late stage becomes so much altered that several degrees of loss are registered when the thermometer is put in the cleft between the little and ring fingers of the injured hand, we are quite unable to call in to our aid any theories of altered blood supply. The vaso-motor is uninjured, and the arteries supplying the cooled part are branches of the same trunk which feeds others which remain warm." [1]

It has been suggested that the profound modifications of temperature caused by injuries of the cervical cord, are really due to altered conditions of the circulation, consequent on injury of the vaso-motor centres; and that paraylsis of the inhibitory function of that centre, by causing increased fulness of the cutaneous vessels, leads to increased elimination of heat, and consequent lowering of the temperature of the whole body. In the more numerous cases in which there is the opposite condition—a great rise of temperature—the result is attributed to increased activity of the heat-producing processes.

But to say that there is increased activity of the processes by which heat is produced, is to indicate, not to explain, the rise of temperature. What we want to know is why, in such injuries, these processes are more active, and why this increased activity on their part is not counterbalanced by a corresponding increase in heat discharge.

It is quite evident that no altered condition of the circulation, and not even the most extensive and violent inflammation, could, in a few hours, raise the temperature twelve or thirteen degrees above the normal standard; it is equally certain that no amount of ordinary tissue change could produce such a result.

There is no reason why, in injuries of the cervical cord, tissue change should be more active; and there is no evidence of its being so.

Neither is there any apparent reason why, in such injuries, the ordinary heat-eliminating action of the cutaneous surface should cease, and heat accumulate in the system; for the physical condition and relation of the skin and of its environment are unchanged.

In short, it is impossible to explain the great alteration of temperature, resulting from injury to the cervical cord, by a reference to any of the ordinary physical causes of heat production and elimination.

The conclusion is forced upon us, that the great rise of temperature

---

[1] Hutchinson, loc. cit.

which accompanies such injuries, is essentially associated with the *seat* of the injury, and not with its nature or extent; for similar injuries in other parts of the cord produce no such effect.

To regard injury of a limited portion of the nervous centres as being *per se* a cause of a great rise of temperature (as we unquestionably do regard injury of the cervical cord), is to invest the injured portion with a heat-modifying power, which is quite above, and distinct from, the results of tissue change and surface transpiration. It is, in short, to recognize the existence in it of a special thermic centre.

Such a centre can have but one function—to control and regulate the production and elimination of heat.

The blood plays such an important part as a distributing agent, that the centre which controls heat distribution is likely to have some working relation with that which controls the distribution of the circulating fluid. The vaso-moto centre and the thermic centre are, therefore, likely to have their seat in the same part of the nervous system. The former, we know from the experience of Ludwig, Schiff, etc., has its seat in the cerebral and spinal medulla. The latter, there is reason to believe, has its seat in or about the same locality.

Seated in the same part of the nervous system it is all but inevitable that injury of that part should cause disturbance both of the vaso-motor and thermic centres—the former evidenced by marked changes in the circulation, the latter by marked change of temperature.

The great change of temperature noted in injury of the cervical cord, has no essential connection with, or causal relation to, the altered condition of the circulation, which is sometimes associated with it. Both are to be regarded as conjoint results of injury to the upper part of the cord—the seat of both the vaso-motor and thermic centres.

Our position, then, is as follows:—

We believe (1) that there is a special thermic centre, seated probably high up in the cord, controlling and regulating the temperature of the body; (2) that this centre is endowed with heat-producing and heat-inhibiting powers; (3) that it has intimate physiological and anatomical relations with other important centres; (4) that it has connected with it a special set of thermal nerves, distinct from the ordinary nerves of sensation; (5) that these nerves are very freely distributed to the skin.

The thermal apparatus thus consists of a central, and a peripheral portion. Each is essential to the functional completeness of the other. Impressions pass from the central to the peripheral, and from the peripheral to the central.

How profoundly the temperature of the body may be altered by central lesions, is evidenced by what is noted in connection with injuries of the cervical cord.

What we have now to do, is to explain the occurrence of a similar change independently of such a lesion.

Besides central lesions, peripheral impressions form the only means by which disturbance of the thermal apparatus could be produced.

It is quite possible that such impressions — that is, impressions originating on the cutaneous extremities of the thermal nerves, and transmitted thence to the thermic centre—might be sufficiently powerful and prolonged to produce serious disturbance there, and even cause such rise of temperature as is noted in connection with central lesions.

The question before us thus narrows itself into a consideration of the point as to whether or not, in the diseases in connection with which hyperpyrexia occurs independently of central lesion, there exists any cause of peripheral disturbance, competent to produce such a result.

The only two morbid conditions in connection with which such hyperpyrexia is habitually found to occur, are heat-stroke and acute rheumatism.

The question thus further narrows itself into a consideration of the point as to whether or not, in heat-stroke and acute rheumatism, there exists any cause of serious disturbance of the thermal peripheræ.

It is evident that in both of these there may be considerable disturbance of the cutaneous thermal peripheræ; for in the one there is always exposure of the surface of the body to a high temperature, and the other has for one of its prominent characteristics, unsually free action of the skin.

The hyperpyrexia of acute rheumatism cannot be rightly considered without reference to the same condition as it presents itself in heat-stroke. The conjoint consideration of these two morbid conditions cannot fail to force on our attention their strong resemblance to each other. The morbid condition which most resembles rheumatic hyperpyrexia, is heat-stroke; the morbid condition which most resembles

heat-stroke, is rheumatic hyperpyrexia. In both, the prominent symptoms during life, are great rise of temperature, alarming nervous symptoms, and a tendency to a speedily fatal termination. In both, the only constant *post-mortem* features, are a tendency to rapid decomposition of the body, a fluid condition of the blood, and more or less congestion of the lungs. Indeed, apart from differences in their history —involving in the one case, exposure to a high temperature, and in the other the prior occurrence of rheumatic symptoms—the description of the one might almost apply to the other.

The circumstances which lead to the occurrence of the hyperpyrexia of heat-stroke, being so much more apparent than those which lead to the onset of the same symptom in acute rheumatism, a brief consideration of its mode of production in the former, may usefully precede our inquiry into its causation in the latter.

Heat-stroke is produced in one of two ways: either by the direct action of the sun's rays on the head and upper part of the spine; or by a more prolonged exposure of the whole body to a high temperature, with or without any direct action of the sun. The former is a veritable sun-stroke—a true *coup de soleil;* the latter a heat-stroke, properly so-called.

In considering the pathology and mode of production of heat-stroke, allowance must be made for these two different forms of heat action. For though the morbid state to which each gives rise may be practically the same, there is a considerable difference in its mode of production in the two cases.

In *coup de soleil,* due to direct exposure to the sun's rays, the patient is struck down without previous warning, and the seizure is rightly attributed to the direct action of the sun's rays on the head and neck. That it is thus produced, is evidenced by the fact that the accident may be guarded against by proper protection of these parts.

Sunstroke, thus induced, varies in severity. The seizure may be so violent as to prove almost immediately fatal; or recovery may be more or less complete. The symptoms vary with the severity of the stroke, and with the extent of the nervous lesion. If the cerebrum is mainly affected, the symptoms will be chiefly those of cerebral disturbance; if

the upper part of the spine suffer, the functions of organic life will be interfered with and the danger to life be correspondingly great.

The thermic centre, we have seen reason to believe, has its seat in the cervical cord. In the history of sun-stroke, there is no fact better established than that protection of the back of the neck is as important as protection of the head; and all the coverings and head-pieces used by Europeans resident in tropical climates are so constructed as to afford this double protection: it being universally recognized that exposure of the back of the neck is as hazardous as exposure of the head.

The hyperpyrexia which occurs in cases of sun-stroke thus induced, is due to the direct action of the sun's rays on the insufficiently protected thermic and other centres; and is, both etiologically and pathologically, more allied to that which occurs in connection with lesions of the cord, than to that which occurs in connection with acute rheumatism.

It is otherwise with the more slowly induced heat-stroke, due to prolonged exposure of the whole body to a high temperature. Here there is no special exposure of the head or neck; and the seizure may come on during the night as well as during the day. It is more apt to occur when, with exposure to heat, there is combined exhaustion from fatiguing exercise—as in soldiers after a long march. Its occurrence, too, is favored by anything which interferes with the free play of the lungs, such as tight or unsuitable clothing; or by anything which prevents these organs from performing their function aright, such as breathing a vitiated atmosphere.

Such are the facts. How are they to be interpreted?

That prolonged exposure to a high temperature is likely, in a native of a temperate climate unaccustomed to such exposure, to cause some disturbance of the thermal apparatus, there can be no doubt. Heat is a normal product of tissue change, ranking in this respect with urea and carbonic acid, and, like them, requiring to be eliminated. Its chief channel of elimination is the skin. Anything which interferes with this heat-eliminating function, may lead to the retention of heat in the system. And thus the atmosphere of a tropical climate might act. For just as an excess of carbonic acid in the atmosphere is a bar to the elimination of that gas from the system, so the presence in the atmosphere of an undue amount of heat is a physical obstacle to

the ready elimination from the body of the heat formed therein. Thus, prolonged exposure to a high temperature might lead to the retention of heat in the system, and mere residence in a tropical climate be a cause of disturbance of the thermic centre.

But there is a safeguard against this; for the same cause which makes the elimination of heat more difficult, produces also increased action of the skin: and this latter effect is a counterbalancing agency to the former. The possibly injurious effects of such prolonged exposure to heat as is inseparable from residence in a hot climate, are thus met by increased activity of the heat-eliminating surface.

It is evident, however, that under such circumstances the due quantity of heat can be eliminated only by increased effort of the eliminating apparatus; and that the inhibitory function of the thermic centre must be very actively stimulated. The stimulation must indeed at times amount almost to irritation, so great are the obstacles to the efficient performance of its function. Such irritation might be so great as to cause considerable disturbance of the thermic centre, and so tax its heat-inhibiting power as to render it incapable of responding to any increased call—such, for instance, as that which would result from vigorous or prolonged muscular exercise; or that which would follow interference with the action of the lungs—the other channel of heat elimination.

It is probable that this is what really occurs in cases of heat-stroke. There is considerable and constant irritation of the peripheral portion of the thermal apparatus—an irritation which must be transmitted to the central portion, producing there an amount of disturbance which may not suffice to cause disorder, but which may be enough to tax to the utmost its heat-inhibiting power, and render it incapable of responding to any increased call. Under such circumstances, increased exposure to heat, as to the sun's rays; a few hours' exercise; or a night spent in a badly ventilated room, might upset the already tottering balance, and produce more or less complete paralysis of the heat-inhibiting centre. The heat-producing portion of the thermic centre being thus left in uncontrolled possession of the field, the temperature would speedily run up, and hyperpyrexia result.

There is no difficulty in understanding how heat might produce such a result, if we only regard it as an excretory product, requiring to

be eliminated. Just as excess of carbonic acid in the blood stimulates the respiratory centre, and leads to increased force and frequency of respiration—so an excess of heat stimulates the thermic centre, and leads to increased activity of the heat-eliminating process.

If stimulation of the respiratory centre be carried beyond a certain point, it results in paralysis; respiration gradually ceases, and the animal dies asphyxiated. So it is with the thermic centre—if its stimulation be carried beyond a certain point, it may result in paralysis of its heat inhibiting or eliminating function, and consequent hyperpyrexia.

That heat elimination is diminished in heat-stroke before the onset of alarming symptoms, is evidenced by the fact noted by Morehead[1] and others, that the seizure is apt to be preceded for some days, not only by headache, giddiness, and other evidence of disturbance of the nervous centres; but by a dry and unperspiring condition of the skin—a condition which clearly points to serious interference with its eliminating function.

The essential difference between sun-stroke due to the direct action of the sun's rays, and heat-stroke resulting from exposure to a high temperature, is that the former results from the direct action of the sun's rays on the thermic centre; while in the latter, that centre is acted on only indirectly through a more prolonged disturbance transmitted to it from its peripheral portion. It is with the latter that the hyperpyrexia of acute rheumatism has analogies.

But, it may be said, if the action (direct or indirect) of heat on the thermic centre be the cause of the disturbance, why is it that only the inhibitory portion of that centre is affected, and that the heat-producing part is not also paralyzed? The answer is simple. Production is a higher function than elimination, and requires for its performance greater power and more vigor. The part of the thermic centre which presides over heat-production is, therefore, likely to be possessed of a more robust vitality than that which controls inhibition; and especially is this likely to be the case in a native of a temperate climate, in which the habitually low temperature of the atmosphere not only calls for vigorous heat production, but also greatly favors and facilitates heat elimination. Being possessed of less vitality, the heat-inhibiting

[1] Morehead, Clinical Researches on Diseases in India, 1856.

portion may be seriously affected by an agency which has little or no effect on the heat-producing.

When the function of the whole thermic centre is in abeyance, as in severe crushing of the cord, heat production and heat elimination are both put a stop to. So far as its relation to its environment is concerned, the body is, under such circumstances, in nearly the same position as if life had ceased. Its temperature tends to become that of the surrounding atmosphere; and is prevented from doing so only by the continuance of those tissue changes which go on while life lasts. In other words, the temperature falls, as in Mr. Hutchinson's case already referred to.

One of the prominent results of our inquiry into the pathology of heat-stroke, is the inference that disturbance of the thermic centre, sufficient to cause more or less complete paralysis of its inhibitory function, and consequent great rise of temperature, may be produced by irritation of the peripheral extremities of the thermal nerves. In the case of heat-stroke, the irritant cause is prolonged exposure to a high temperature under unfavorable circumstances.

If any other agency were capable of giving rise to similar irritation of the cutaneous surface, it might lead to a like result. And our inquiry into the causation of the hyperpyrexia of acute rheumatism, involves the consideration of the question as to whether or not there is at work in that disease any cause competent to produce such disturbance of the thermal peripheræ as might upset the thermic centre.

One of the prominent features of an attack of acute rheumatism is excessive action of the skin—the same result which habitually follows prolonged exposure to a high temperature. The cause of the profuse perspirations of acute rheumatism, is the presence in the blood of an excess of lactic acid. This acid has, on the cutaneous surface, even a more decidedly stimulant action than a hot atmosphere. Except heat-stroke, acute rheumatism is the only disease in which such excessive stimulation of the cutaneous surface is constant and habitual: except heat-stroke, it is also the only one in which hyperpyrexia is habitual. If we regard the hyperpyrexia of heat-stroke as an indirect result of excessive stimulation of the cutaneous surface, we can scarcely avoid the inference that the hyperpyrexia of acute rheumatism may be simi-

larly associated with the excessive action of the skin, characteristic of that disease—that lactic acid may cause in acute rheumatism, not only the same disturbance of the cutaneous surface which results from exposure to the atmosphere of a tropical climate, but may also indirectly produce a like disturbance of the thermic centre. Certain it is, that if excessive and prolonged irritation of the whole cutaneous surface, and its contained thermal peripheræ, may cause disturbance of the thermic centre, we have at work in acute rheumatism an agency competent to produce such a result.

The disturbing effect of lactic acid is exercised primarily on the water-eliminating function of the skin—that of a tropical atmosphere on the heat-eliminating; but the two functions are so inseparably associated, that stimulation of the one necessarily involves stimulation of the other. Thus we have at work in acute rheumatism an agency similar to that which operates in heat-stroke, and to whose indirect action we believe the hyperpyrexia of this latter to be attributable: and thus the inference is presented to us, that the hyperpyrexia of acute rheumatism, like that of heat-stroke, may be due to disturbance of the thermic centre, consequent on irritation of the thermal peripheræ.

2. *The relation of the high temperature to the brain symptoms, and the fatal result.*

There are two views on this point. According to one, the high temperature is primary, and the nervous symptoms secondary; according to the other, the nervous disturbance is primary, and the high temperature secondary.

According to the former, which has been advocated by Liebermeister[1] and others, the high temperature causes disturbance, and ultimately paralysis, of the nervous centres. The chief evidence in support of this view, is the frequent association of nervous symptoms with an unusually high temperature.

In acute rheumatism a very high temperature is always accompanied by such symptoms; but it is not so in all diseases. Reference has already been made to a case recorded by Mr. Teale in which a temperature of 122° produced no serious disturbance. The case is so unique, that one does not care to do more than merely refer to it. But in re-

[1] Deutsch. Arch. für Klin. Med., Vol. I., 1866.

lapsing fever it is not uncommon to find the body heat run up to 106°, 107°, and 108°, without giving rise to any disturbance of the nervous centres. "High temperatures in relapsing fever entail little or no danger to the patient, and do not produce serious nervous symptoms. Of Obermeier's patients the temperature of three rose to 107.6°, of six to 107.7°, and of two to 108.5°. In all these cases no special danger attributable to the high temperature could be discovered, nor even a single circumstance in which they differed from the rest." "During the attacks," says Tennent, "the height attained by the temperature was on an average between 104° and 106°. In many cases, however, it was found to be as high as 107°, while in two cases 108° was noted. In these cases of very high temperature, the condition otherwise was not in any way notably different."

Of all the continued fevers, relapsing fever is the one in which the body heat has the highest range, and in which the temperature of hyperpyrexia is most frequently noted. Did a high temperature of the blood have, on the nervous centres, the disturbing influence that Liebermeister and others believe it to have, head symptoms would be a prominent feature in relapsing fever. But the reverse is the case; for they are much less marked and frequent in it than in typhus and typhoid fevers, in which the body heat is, as a rule, less elevated.[2]

In acute rheumatism a temperature of 107° or 108° is always accompanied by alarming nervous symptoms; but with such an absolute demonstration as that afforded by the case of relapsing fever, that this rise may cause no unusual symptoms, it is impossible to accept the view that in rheumatic hyperpyrexia the high temperature is the cause of the nervous disturbance.

There is ample evidence to show that lesions of certain parts of the nervous centres may cause an unusual rise of temperature. There is not sufficient evidence to show that unusual elevation of the body heat may cause disturbance of the nervous centres.

---

[1] Murchison, On the Continued Fevers of Great Britain, 2nd ed., p. 356.

[2] A temperature of 106° to 108° occurring in relapsing fever is an ordinary feature of the disease. It is produced by the propagation of the contagium in the blood, in the same way as the ordinary pyrexia of acute rheumatism. For a detailed account of the mode of production of the pyrexia of the continued fevers, the reader is referred to the author's work on The Germ Theory of Disease, already referred to.

In rheumatic hyperpyrexia there are both high temperature, and serious nervous symptoms: in relapsing fever there is only high temperature. It is evident that the state of matters with which we have to deal in rheumatic hyperpyrexia, resembles that which presents itself in relapsing fever with high temperature, less than it does that noted in lesions of the upper part of the cord, and in these there can be no doubt that the high temperature is secondary to the central lesion.

Moreover, it is incumbent upon us to explain the occurrence of the high temperature. But, on the view that it is primary, how are we to do so? In the absence of prior disturbance of the nervous centres, what possible reason is there for the rise? Absolutely none. And surely no view of the mode of production of the general condition to which we apply the term hyperpyrexia, can be accepted as adequate, which does not even attempt to explain one of its most prominent and characteristic features.

Those who regard the high temperature as the cause of the nervous symptoms of rheumatic hyperpyrexia, have committed the same fatal error that was made by the advocates of the lactic acid theory—they have taken one of the symptoms of this condition, and have raised it from its subordinate position of a symptom, to the rank and dignity of an exciting cause.

It is evident that the view that the nervous symptoms of rheumatic hyperpyrexia are caused by the high temperature, lacks the support which would commend it to our reason.

The alternative view, that the high temperature is secondary to disturbance of the nervous centres, more readily commends itself to us. There is not only no distinct evidence that a high temperature of the body ever causes disturbance of the nervous centres: but there is distinct evidence, first that such temperature frequently occurs without any such result; and second, that disturbance of the nervous centres may cause unusual rise of temperature.

If we acknowledge the existence of a connection between the high temperature and the nervous symptoms of rheumatic hyperpyrexia, we must, in the light of such evidence, accept the view that the high temperature, and the alarming symptoms which accompany it, are associated together, not as cause and effect, but as conjoint results of some disturbing influence acting on the nervous centres.

It has already been shown how disturbance of the thermic centre, and consequent great rise of temperature, might be indirectly brought about in acute rheumatism by the irritant action of lactic acid on the thermal peripheræ.

If the thermic centre be situate, as we believe it to be, in or about the spinal medulla, it is situate in a part of the nervous system which is also the controlling centre of the most important functions of organic life. Any serious interference with the functional integrity of these centres, must be accompanied by alarming symptoms, and danger to life. Thus it is that a high temperature in acute rheumatism is accompanied by such alarming symptoms, and so great danger. Situated as it is, at the upper part of the cord, and intimately associated as it is, both anatomically and physiologically, with other important centres, the thermic centre cannot be seriously disturbed without there being produced also some disturbance of the vaso-motor, nutritive, cardiac, and respiratory centres, situate in its immediate neighborhood, and possibly in direct contact with it. The greater the disturbance of the thermic centre, the greater would be, not only the rise of temperature, but the participation of contiguous centres in that disturbance. Hence the greater the rise of temperature, the greater the danger to life—not because the high temperature is in itself a danger, but because what induces that symptom causes also other and more serious ones. The prominence of all the effects is directly as the extent of the causal disturbance.

The results of *post-mortem* examinations of fatal cases of rheumatic hyperpyrexia, are in keeping with this view of its mode of production. Functional disturbance of such important centres as those involved, might cause a fatal result, without leaving behind any lesion recognizable after death, and thus might be explained the negative results of examination of the nervous centres. The congestion of the lungs, which is so commonly noted, might, and probably does, result from disturbance of the vaso-motor, respiratory, and cardiac centres. The fluid condition of the blood points to disturbance of the nutritive centres. While the only other constant *post-mortem* feature, unusually rapid decomposition, is attributable to the high temperature of the body at the time of death and for some hours afterwards. Decomposition is more rapid in the body of a man dead of rheumatic hyperpyrexia,

than in one dead of an ailment involving no excessive body heat, for the same reason that it is more rapid in a hot than in a cold climate. Heat promotes such decomposition.

The relation which rheumatism bears to hyperpyrexia, is very like that which it bears to chorea. When considering this latter point we saw (1) that rheumatism was essentially a disease of the motor peripheræ, and chorea essentially a disease of the motor centres; (2) that the motor apparatus affected in rheumatism has an essential and intimate functional connection with the motor centres; and (3) that those whose motor peripheræ were liable to rheumatic disturbance, were more likely to suffer occasionally from disturbance of the motor apparatus, than those in whom no such liability existed.

After the joint affection, one of the most characteristic features of acute rheumatism is the free action of the skin. This involves, as we have seen, possible disturbance of the thermal peripheræ. Now, just as a rheumatic subject is more liable than a non-rheumatic to have his motor centres disturbed, and the symptoms of chorea result—so also is he more likely to have his thermic centre disturbed, and the symptoms of hyperpyrexia result: disturbance of the thermal peripheræ predisposing him to hyperpyrexia, just as disturbance of the motor peripheræ predisposes him to chorea.

But the question naturally arises—if the hyperpyrexia of acute rheumatism be due to disturbance of the thermic and neighboring centres, and if this disturbance be an indirect result of the action of lactic acid on the extremities of the thermal nerves, why is it that it occurs in only a small percentage of cases of acute rheumatism? The stimulant effect of lactic acid is got in every case of that disease; in every case, therefore, it may be said, there ought to be hyperpyrexia, if its mode of production were such as we suppose.

This objection is the same as that with which we had to deal when explaining the head symptoms of pericarditis, and the relation of rheumatism and chorea. These, we saw reason to believe, were to be accounted for, not by any peculiarity of the rheumatic attack, but by some peculiarity of the individual in whom it occurs.

The same explanation is applicable to rheumatic hyperpyrexia. Prior to the occurrence of the hyperpyrexia, there is nothing in the

case to induce one to expect it; or to distinguish the attack from the dozens of similar ones in which no such disturbance takes place. Failing any peculiarity of the case to account for the exceptional symptoms, we can only refer them to some peculiarity of the affected individual. Indeed, an exceptional symptom, especially when that symptom is of nervous origin, is generally due to some peculiarity of the patient.

Just as it is only in a minority of people that the sensorium is so susceptible as to have its balance upset by the onset of pericarditis, and the motor centres sufficiently susceptible for the production of chorea —so it is only in a small percentage of rheumatic subjects that the thermic centre is so susceptible as to be disturbed, and have its balance upset, by such irritation of the thermal peripheræ as occurs in acute rheumatism.

That the thermic centre may be profoundly affected by influences applied to the thermal peripheræ, and that the hyperpyrexia of heat-stroke, and of acute rheumatism, are thus induced, is further evidenced by the results of the treatment of that condition.

It has been abundantly shown in the case of the hyperpyrexia of heat-stroke, that the treatment which affords the best chance of recovery, consists in applying cold to the extremities of the thermal nerves.

"The principle of management is to reduce as quickly as possible the blood heat. This is best effected by rubbing the body over with ice."[1]

It has been shown, too, first and chiefly by Dr. Wilson Fox,[2] that the hyperpyrexia of acute rheumatism calls for the same treatment; and that the immersion of the body in cold water, or the application of ice to its surface, serves not only to reduce the temperature, but to allay, and ultimately get rid of, those alarming symptoms which are associated with it, and threaten a speedily fatal termination.

The view that has been advanced as to the mode of production of the high temperature in rheumatic hyperpyrexia, and of the alarming symptoms which accompany it, affords a rational foundation for this treatment, and an explanation of its success.

If disturbance of the thermic centre be the cause of the hyperpyrexia; and if this disturbance be, in its turn, induced by irritation of

[1] Aitkens, Practice of Medicine. [2] Treatment of Hyperpyrexia.

the peripheral extremities of the thermal nerves, it is evident that the symptoms thus induced are likely to be best met by the application to the same nerves of an agency having on them an action the reverse of that which caused the disturbance. To allay the disturbance of the thermal apparatus is the object in view. Cold is the means best calculated to attain this end. We know what a quieting influence this agency exercises on the nervous system, and that its prolonged application may even cause alarming depression. Its calming and depressing influence on the nervous centres is evidenced by what is observed in those who are long exposed in a very cold atmosphere. A marked tendency to sleep is one of the early indications of danger. So powerful is this tendency, that it can with difficulty be resisted even by those who are aware that, if they once give way to it, the sleep will deepen into fatal coma.

The beneficial action of cold in hyperpyrexia is generally supposed to be a direct result of the lowering of the temperature of the body. But to suppose that the mere lowering of the body heat is sufficient to allay the alarming symptoms, is equivalent to saying that these symptoms are a result of the high temperature; and *that*, we have already seen, is a position which cannot be maintained.

A more probable explanation of the good effects of cold I believe to be, that it acts directly on the extremities of the thermal nerves; and that the quieting influence there produced is transmitted along these nerves to the thermic centre. If kept up for a sufficient time, this influence, like the prior irritation, is communicated to the neighboring centres. And thus, as a consequence of the direct action of cold on the peripheral extremity of the thermal apparatus, there is produced, either by stimulation of the inhibitory, or paralysis of the producing, portion of the thermic centre, a restoration of the balance of these two antagonistic agencies, and an amelioration of all the symptoms which resulted from its disturbance.

Cold seems to allay the alarming symptoms by lowering the body heat, just as the high temperature seemed to induce them. But just as the elevation of the temperature was secondary to, and consequent on, the disturbance of the nervous centres; so it is probable that its restoration to the normal under the influence of cold, is chiefly attributable to the quieting influence of that agency on the disturbed thermic

centre. A certain amount of heat, of course, passes off from the surface; but the cold which passes in (if I may so express it) is the real curative agency. By the cold which passes in, I mean the influence transmitted from the cold surface along the thermal nerves to the thermic centre.

INDEX.