

## **On the treatment of acute rheumatism by salicylate of soda.**

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ON THE  
TREATMENT OF ACUTE RHEUMATISM  
BY SALICYLATE OF SODA.

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BY SEYMOUR JOHN SHARKEY, M.B.,  
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ALTHOUGH a large number of cases of acute rheumatism treated by salicin and its compounds have been published, it may be useful to give the results of this method of treatment as carried out at St. Thomas's Hospital, quoting only exceptionally cases in detail. The remarks made are to be taken simply as products of an experience confined to this hospital. The cases thus treated during the past year have been very numerous, and I have personally taken notes of about forty, which together with the impressions made upon me by the rest are the basis of the statements made below.

Some cases were treated with salicin, some with salicylic acid, but in the great majority salicylate of soda was employed; for the latter not only has the advantage of being readily soluble in water, but it seems also to be more effectual than the other two. At first 30 grains every two or three hours was the quantity prescribed; but latterly 20 grains repeated at the same intervals have been found to answer the purpose equally well, and to be capable of being taken with less chance of unpleasant results. Smaller quantities than these, however, are rarely effectual in the adult.

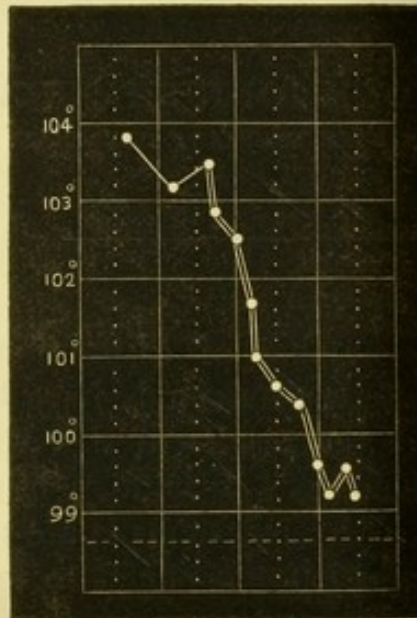
The following may be taken as an example of a successful case. (See Temperature Chart I.)

James F—, æt. 27, was admitted into Charity Ward, under Dr. Bristowe, on January 12th, 1878.

He had had four previous attacks of rheumatic fever, the first at the age of seventeen, and the last a year ago. He had always had good health in the intervals between the attacks, and had never suffered from symptoms of cardiac disease. During the month previous to admission he had had a cough

CHART I.

<i>Date.—January</i>	12	13	14	15
<i>Day of disease</i>	6	7	8	9



Salicylate  
of soda.

N.B.—The period of taking salicylate is indicated by a double line.

and cold, and six days before admission he was seized with pains in the ankles, which subsequently affected the knees, shoulders, and left arm.

On the night of the 12th he had no sleep on account of pain in the joints, and on the morning of the 13th he had pain in the ankles, knees, shoulders, left elbow, and wrist, and all these joints were somewhat swollen. The tongue was thickly furred, white, and moist; the bowels had been confined for three days; the appetite was bad, and the patient very thirsty

The temperature was  $103^{\circ}$ — $104^{\circ}$ , and the skin perspiring ; pulse 112 ; respiration 28.

Cardiac dulness was normal in extent, the sounds muffled, but there was no murmur. The lungs were resonant throughout, and there was a little crepitation at both bases.

Urine sp. gr. 1028, high coloured, clear, and contained a small quantity of albumen. One pint eleven ounces had been passed in the last twenty-four hours.

The temperature, which had been taken several times since admission, remained between  $103^{\circ}$  and  $104^{\circ}$ , and the patient was ordered at 1.30 p.m. on the 13th to take—

Sodæ Salicyl., gr. xx ;  
Syrupi Aurantii, ʒj ;  
Aquæ destill., ʒj.

and the medicine to be repeated every three hours.

April 14th.—Had a very good night ; the pain was easier after the first dose, and is gone this morning. The patient has perspired very profusely, much more so than before he took the medicine, and is a little deaf. Temp.  $101^{\circ}$  ; pulse 100 ; resp. 32.

The urine which he passed four and a half hours after taking the first dose gave a deep purple coloration on the addition of a solution of perchloride of iron, showing the presence of a salicylic compound. No evidence of cardiac or pulmonary disease. The urine contains about the same quantity of albumen.

15th, a.m.—Bowels not open since admission, notwithstanding his having taken purgative medicine ; tongue very thickly coated. No pain. Temp.  $99.2^{\circ}$ . Is somewhat deaf, and has "sounds like music" in his ears. Perspiring very freely ; slept well, dreaming however a good deal. No nausea or sickness. Pulse 96 ; resp. 28. Urine in the last twenty-four hours one pint seven ounces. The patient appears fidgetty and nervous, and looks somewhat wild, as they often do when beginning to suffer from salicylic poisoning.

P.m.—Bowels open.

At 4 p.m. the medicine was stopped.

16th.—Fidgettiness much less ; did not sleep quite so well ; still a little deaf, but no noises in the ears ; perspiration much less profuse.

In the last twenty-four hours one pint and three quarters of urine passed of sp. gr. 1038. No albumen; marked reaction with perchloride of iron.

The temperature never rose again, and the patient had no return of pain or other rheumatic symptoms, and was discharged on January 28th. The salicylic acid disappeared from the urine seventy-one hours after the last dose was taken.

The patient took sixteen doses of the medicine in the two days, making in all 320 grains.

When the drug is given in these quantities the first result usually is diminution of pain, and so rapid is this that it often follows the first or second dose. With it the temperature also is reduced, and there is profuse perspiration. The patient generally complains too of deafness and noises in the ears. These effects are pretty constant, and may be accompanied by nausea or even vomiting, so that the medicine has to be stopped; the latter, however, is rather an exceptional occurrence. The swelling and redness leaves the joints much less rapidly than the pain, and the tongue often remains furred long after the patient feels quite comfortable, and is almost free from fever.

Salicin has the advantage of producing to a far less extent, and often not at all, the unpleasant phenomena which are pretty constant when salicylate of soda is given; but its power of reducing the temperature seems to be much smaller than that of the salicylate, even when given in the same quantities.

A not at all uncommon accompaniment of the internal use of salicylate of soda is a profuse miliary eruption, which very often becomes pustular. Sometimes vesicles of a considerable size, filled with pus, are distributed over the body, and even a succession of very troublesome pustules may result. The greater frequency of the miliary eruption when this treatment is employed, and its greater proneness to suppuration, make it probable that it is in some way due to the salicylate, especially when we remember what profuse diaphoresis is produced by the drug. In one case a general erythema preceded the miliary eruption, and in another urticaria occurred, but I have only seen one case of each.

In some cases the drug seems to affect the nervous system more especially, and delirium may be very rapidly produced.

In other cases nervous symptoms do not supervene until a considerable quantity of the salicylate has been taken. Rapidly supervening delirium is not so common as that produced after a while, and when it does occur it is often exceedingly violent. A curious circumstance is that if in such a case the medicine be stopped until the delirium has passed off, and be then again administered, the patient sometimes takes it without any recurrence of cerebral symptoms.

The delirium which occurs after a considerable quantity of the drug has been taken may, or may not, be violent; it is generally preceded and accompanied by great restlessness, rapid breathing, and dryness of the tongue. The patient dreams, and has varied hallucinations. One patient, for instance, thought he had left the hospital and had gone to a theatre, where he saw duelling going on and people advancing to kill him, and the entrance to the ward appeared like a lighted tunnel. Still, however unpleasant the immediate consequences of the administration of the drug to patients who take it badly, these all rapidly subside after it is left off, and no permanent injury is done.

It is at present impossible to distinguish those cases who are likely to take the medicine with rapidly good effect, and without any unpleasant results from those who are intolerant of it. But it may be stated that persons in great pain, and with high fever, and in whom there is not, when the treatment is commenced, any complication, are, as a rule, the most favorable cases for it. Still slight complications, whether cardiac or pulmonary, should not preclude the treatment by salicylate of soda. Indeed, cases occur in which the drug produces rapid relief of the pain and joint affection, and no unpleasant symptoms whatever, notwithstanding the presence of pretty serious complications. Usually, however, the drug seems to have very little effect in modifying the course of cardiac or pulmonary affections occurring in acute rheumatism, although it may reduce the temperature in spite of them.

A girl of eighteen, for instance, had been in the hospital under Dr. Murchison for five days, with a temperature which ranged generally from  $101^{\circ}$  to  $103^{\circ}$ . Salicylate of soda was then given, which reduced the temperature to  $97.8^{\circ}$  in about fourteen hours. The medicine was then stopped, and on the

third day from that time an acute pneumonia of the right lung, pericarditis, and pleurisy on the left side made their appearance. Twelve hours after these complications were discovered the temperature was still  $98.6^{\circ}$ , and in twelve hours more the girl died with her temperature below  $100^{\circ}$ , but with a pustular miliary eruption, pericarditis, left pleurisy, and consolidation of a large part of the right lung.

When the treatment is commenced before any secondary affections have made their appearance, the probabilities of their doing so are, of course, very greatly diminished, but they are not even under such circumstances necessarily prevented, for both cardiac and pulmonary diseases have arisen in several cases while the system was saturated with salicylate of soda.

The question of the production of albuminuria by the salicylate is one which has received some attention, and it has even been suggested that the delirium may be due to this cause. There is no doubt that occasionally albumen makes its appearance in the urine after the treatment has been commenced; but the facts—that in the great majority of cases it does not do so; that in many cases in which albumen is present before the drug is given it disappears during its administration; and, finally, that albumen is frequently present in the urine of rheumatic patients with high temperature before any treatment whatever has been applied, go far to prove that the albuminuria ordinarily has nothing to do with the medicine.

It is only recently that I have been carefully observing the occurrence of albuminuria in cases of rheumatic fever with a view to determine how far it is a result of the treatment by salicylate of soda. Out of ten cases in which albumen was present, seven had it before the drug was administered, and it disappeared in all these while the urine still gave a strong reaction with the perchloride of iron. In the eighth case the urine was not tested for albumen before the medicine was given, but albumen was found in it and disappeared from it while it still contained the salicylate. In the remaining two cases the urine contained no albumen before the treatment was commenced, but it made its appearance afterwards, and again disappeared while the urine still contained the drug.

At any rate it can be stated with certainty that salicylate of soda, when given in the ordinary doses, never produces perma-

ment albuminuria. That the delirium is not due to albuminuria is equally certain, for in many cases, if not in most, there is no albumen present during the period of delirium. It seems, indeed, probable from the experience of this hospital that the presence of a small quantity of albumen in the urine should be no objection to the treatment by salicylate of soda, as the latter is just as effectual in such cases, and is not more likely to be attended with unpleasant results than in those in which the urine is free from albumen.

The delirium is probably due to the action of the salicylic acid on the brain itself. Of nine cases of delirium occurring during the administration of the drug, of which I have notes, two had neither albuminuria nor complications; two had a very small amount of albumen in the urine and no complications; two had no albuminuria, but had complications; two had no albuminuria, and the presence of complications at the time of the delirium was doubtful, while the remaining one had both albuminuria and complications.

It is, in fact, at present impossible to say in what class of cases delirium does occur, so varied is the condition of patients affected by it.

The liability to relapses after the salicylic treatment is considerable, especially when the drug is suddenly stopped. But if it be continued in much smaller quantities for some time after the temperature is normal, this liability is very greatly diminished.

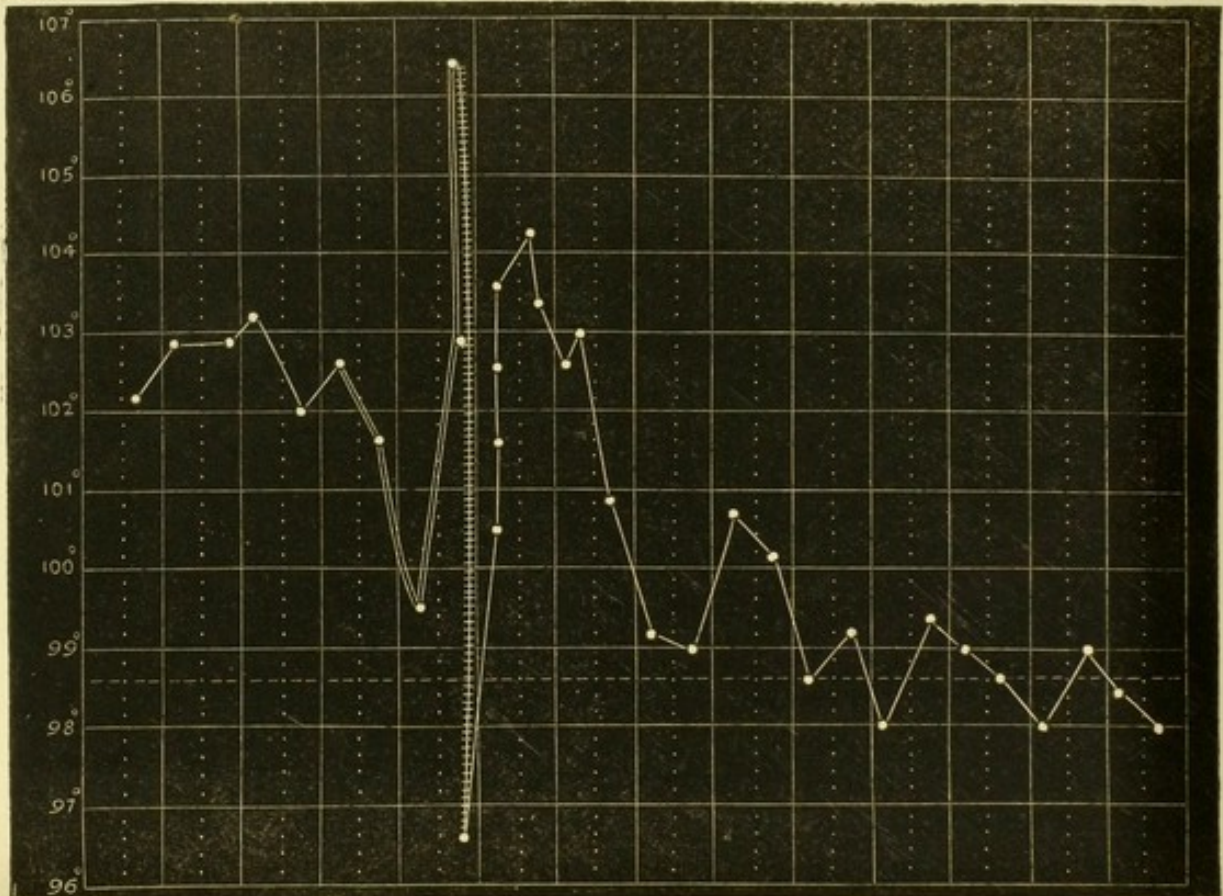
A very curious train of symptoms occurred in three cases of acute rheumatism, which were being treated with salicylate of soda, viz. a very high temperature, accompanied by great restlessness and delirium. In one case these occurred immediately after stopping the drug, and in the other two while the patients were still taking it. In one of these cases there was a considerable quantity of albumen in the urine before the treatment was commenced, but no other complications; in another there was no albuminuria, but a mitral systolic murmur; and in the last there was a trace of albumen, but no other complications. The only character which these cases had in common besides those mentioned above was the presence of a profuse miliary eruption, which became pustular. In one case (that represented in Chart II) the temperature rose to  $106.4^{\circ}$ , in



the second to  $106^{\circ}$ , and in the third to  $105.4^{\circ}$ . In each case a graduated cold bath was given, which not only reduced the temperature to normal (though it rose again to a considerable height) but also put a stop to the delirium, restlessness, and insomnia. All three cases got well pretty rapidly afterwards.

CHART II. (Case of Dr. Bristowe's.)

Day of disease.—4 5 6 7 8 9 10 11 12 13 14 15 16 17



Sali- Bath  
cylate of soda

N.B.—The period during which salicylate was given is shown by a double line; the effect of the bath by a crossed line.

As regards the effect of salicylate of soda on the amount of urine passed, I have not been able to come to any definite conclusion. It seems, however, often to diminish it considerably, and also the total quantity of urea. The percentage of urea, too, is affected in the same way, but to a much smaller extent. These variations are well seen in the charts in which my friend Mr. Theodore Acland has recorded the results of his experiments, and which he has used to illustrate a paper which he

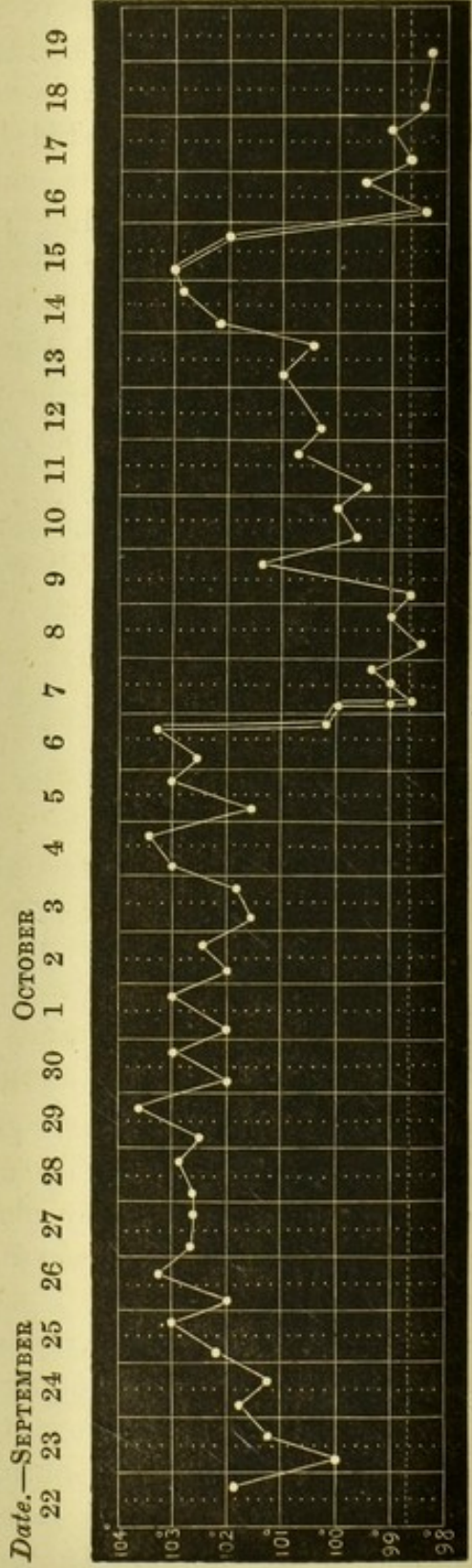
read before the St. Thomas's Hospital Physical Society, reprinted in this volume.

It has recently been asserted that sugar makes its appearance in the urine of persons taking salicylate of soda. To determine this the urine of several patients who had taken large quantities of the salicylate, and whose urine gave a very strong reaction with the perchloride of iron, was tested by boiling with Fehling's solution. At first a precipitate came down, which appeared to be whitish; but on boiling for several minutes longer the whole mixture gradually changed to a reddish-brown colour. This, however, appeared to be due not to any change in the colour of the precipitate, but rather to a change in the fluid. Mr. Theodore Acland then offered to determine whether the precipitate contained copper. The mixture was placed on a filter, and the filtrate came through as a strongly dichroic fluid, olive green by reflected and reddish brown by transmitted light. The precipitate well washed was perfectly white, and dissolved completely in two drops of hydrochloric acid. Ammonia was then added in excess without any colour at all appearing in the fluid, which remained like water, and was consequently free from copper. This showed that the urine had not reduced and precipitated the copper, as it does when it contains sugar.

I then tried the fermentation test. Two test tubes were filled with urine from a case of rheumatic fever, which contained a large quantity of salicylate of soda. In one some German yeast was placed, and in the other none. They were both inverted over mercury, and placed on the ward stove for twenty-four hours. At the end of that time there was hardly any change in the contents of either. When some grape sugar was added to the urine, however, a large quantity of gas was produced by fermentation. It seems then pretty clear that if any sugar at all be present in the urine of these cases its quantity must be infinitesimal.

The drug makes its appearance in the urine very soon after ingestion, but the exact time is not easy to determine, as it may have been excreted by the kidneys long before it is passed from the bladder. In ten cases in which I noted its first appearance, the earliest was one hour and forty minutes after ingestion, the latest eleven and a half hours. In ten cases in

CHART III.



Taking Pot. citratis gr. xxx, træ. Opii m iij, every four hours.

Sodæ salicyl. gr. xx every two hours.

Sodæ salicyl. gr. xx every two hours.

Convalescent.

N.B.—The period during which salicylate was given is shown by a double line in the temperature chart.

This chart shows the rapid effects of salicylate of soda in a case where other treatment was ineffectual. The pain and swelling of joints were reduced rapidly, like the temperature.

which I noted the time of its disappearance from the urine the shortest time was sixteen hours, the longest ninety-six hours. I have found it not only in the urine, but also in the blood, in the serum from blisters, and in the expectoration,—care being taken in the case of the latter to prevent any possible admixture of the medicine as it passed through the mouth. I have on several occasions tested the perspiration of patients whose system was saturated with salicylate of soda, and I have managed to get considerable quantities collected in test tubes for examination, but I have never detected evident signs of the drug in that excretion. This is the more curious as the perspiration is so remarkably increased by this treatment. It is not found in the fluid of hydatids from patients who are taking the salicylate at the time of tapping.

Any one who has seen many cases of acute rheumatism treated by salicylate of soda must, I think, allow that its discovery as a cure for that disease is a triumph of empirical therapeutics, which has probably had but few parallels in the history of medicine. It has now had a fair and extensive trial, and to say that it far excels any other method of treatment would be to give the drug but scanty praise. It may rather be said that until the application of salicin and its compounds to the treatment of rheumatic fever, there was no drug which could be relied upon to shorten, to any great extent, its tedious course. Now, however, making due allowance for cases of failure, which do undoubtedly occur, not only can cessation of the primary phenomena of the disease—pain and fever—be rapidly secured, but we likewise have good grounds for hope, that owing to the remarkable power which the drug possesses of curtailing the duration of the disease, those secondary affections of the heart which make acute rheumatism so serious, may be greatly diminished in number and intensity.

In conclusion I have to thank the physicians, one and all, for very kindly allowing me to make use of their cases for the purposes of this paper.

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