The Treatment of Rheumatic Fever by the Salicyl Compounds

Thesis for the degree of M. D.

by

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The following thesis is based on (1) the clinical histories of a number of cases of rheumatic fever treated in Glasgow Western Infirmary in 1891-92, and (2) the recent literature of the question. I have restricted my examination of the literature to those works and papers which have been published since the middle of 1891, i.e. five years after the introduction of salicin by Dr Maclagan. After being in use for five years a remedy is no longer new and an approach to a precise estimate of its value may then be expected.

In fourteen cases of rheumatic fever treated in the Western Infirmary (ten having been under my own care as House Physician) the general results of treatment by salicin were as follow:

The average duration of apyrexia (i.e. until temperature was below 100°F. during the whole 24 hours) in 12 cases was 6·7 days.

The average duration of pain was 3·7 days.

The average length of stay was 39 days.

Relapses (one or more) were present in 50 per cent of the cases.

In one case no cardiac murmur was noted until the eighth day after admission, while in another the patient was observed to have a V.S. murmur on admission

and on A. S. morning on the fourth day. The latter may have been at first overlooked.

In this summary the duration of pyrexia in three cases has not been included, because in one temperature was still abnormal on the sixth day of treatment with salicin, and quinine was then resorted to, while in the other case alkaline treatment was begun on the ninth day after admission, and temperature did not remain for 24 hours below 100° F. until the thirtieth day. The rest of the statement refers to the whole 14 cases.

The shortest period of pyrexia was less than two days - the next was two days. The longest, with the exception of the cases just mentioned, was fourteen days (in two cases). In two cases the duration was nine days.

The shortest period of pain was one day, the next was 24 to 34 hours, the third less than two days. The longest period was six days (in three cases). In most cases the pain was markedly relieved earlier - the general statement referring to complete or all but complete absence of pain.

Relapses occurred in seven cases, one in four cases, two in two cases, while in the seventh there was one relapse and the pain then became chronic. In another case, not counted as one of relapse, the pain became chronic.

The longest stay in hospital was 80 days, the shortest

14 days. Only one other patient remained less than 21 days, viz. 17 days.

The highest temperature recorded was 104°F. Other readings were 105° and 102·6°.

The treatment was by salicin, given generally in doses of 20 grains every 2 or 3 hours until acute symptoms subsided, and continued as considered necessary. An alkaline tonic was frequently given after the salicin had been discontinued.

The age of patients ranged from 13 years to 54 years. The average was 29 years.

The average duration of symptoms before treatment was begun in hospital (in 12 cases) was 7·16 days. In one case a note of the previous duration had been omitted, and in another (not included) the patient had been suffering more or less for a month.

In 7 cases the attack was said to be the first; in one case there had been two previous attacks; in 5 cases one previous attack.

The age of the patient does not appear to have any bearing on the earlier or later relief of symptoms.

In 7 cases, in which the patient had not had any previous attack, the average duration of pain was 2·6 days; in 6 cases, in which there had been previous attack, the average duration was 4·6 days.

The average duration of hyperia in 6 of the former set (one of the exceptional cases being again excluded) was 4·6 days; in 5 of the latter set 2·2 days. In respect both of relief of pain and of shorter period of hyperia the advantage is on the side of those cases in which there had been no previous attack.

I do not find that there was any special relationship between previous duration and subsidence of symptoms.

Of the seven cases in which relapse occurred there were two only in which there had not been previous attack. As might be expected the average length of stay was higher for those who had relapse, being 50·8 days and 27·5 days respectively.

In one case only was hyperia subdued before pain was fully relieved. In three cases both seem to have been relieved simultaneously. In the cases in which pain was relieved in 30 hours or less hyperia was present for 4 days, 9 days, and 2 days respectively.

There were nine relapses in 7 patients. In five of these there was return both of pain + of hyperia, in one of hyperia only. In one case pain returned before the temperature had become normal. In the eighth case there was return of hyperia and no return of pain is noted, in the ninth pain returned but no return of

"Samuel" II, 1981 pp. 1030, 1090, 1091 + 1119; I, 1982, pp. 9, 64, 134, 135, 188.

pyrexia is continued.

In seven of the cases of relapse patient was not at the time – taking salicin. In two cases (in the same patient) salicin had only been stopped on the day on which the relapse occurred. In two cases the patient was taking salicin. In one case the relapse occurred 17 days after administration of the drug had been stopped, in a second 13 days after, in a third 3 days after. Four patients were undergoing medicinal treatment more or less strongly alkaline; one was taking a quinine tonic.

There does not seem to have been much difference in general results whether dose was given every 2 or every 3 hours after.

None of the cases are appended.

I now propose to bring forward the results of an analysis of such literature, bearing on the question under discussion, as I have been able to find. The most important papers I have met with are those which were read in the debate at the Medical Society of London in December, 1881 and January, 1882, and reported in the "Lancet."

In 463 cases (in different series) treated by the salicyl compounds the range of average duration of ~~temperature~~ pyrexia was 3·75 to 7 days. In 550 cases the range of average duration of pain was 3·75 to 7·25 days.

" Lancet" II, 1991, p. 1030

" . p. 1119

" Lancet" II, 1991, p. 1091

" Lancet" II, 1991, p. 1119

" , p. 1091

The late Dr Hilton Fagge presented the results of treatment in 355 cases, and Dr. Donald Hood these in 350 cases. In 348 of these (or in nearly 50 per cent) pain & pyrexia lasted for 5 days or less; in 176 cases for from 6 to 11 days; in 61 cases for from 12 to 18 days.

Turning now to cases treated by other methods I find that in 124 cases (in different series) the range of average duration of pyrexia was 6·5 to 13·8 days. In 112 cases the range of average duration of pain was 8 to 12 days, i.e. while the average in one series was 8 days, the average in another was 12 days. Twenty-nine of these cases were treated by full doses of alkalis, the result being an average duration of pyrexia of 6·8 days, of pain an average duration of 8 days.

Of 350 cases treated without salicyl compounds only 57 (or 16·3 per cent) lost pain & pyrexia within five days; 114 in 6 to 11 days; 78 in 12 to 18 days.

I think right to note that if one case be omitted from the series presented by Dr Hall and numbering 16 cases the upper limit of the range of duration of pain (in this series) would be 10 days instead of 12 days, while that of pyrexia would be 6·5 instead of 8 days. It is not improbable, however, that this abnormally long may be counterbalanced by one proportionately long in the salicyl series.

Comparing the results in my own short series

I find that the average duration of pain is rather more than half that of the non-salicyl series, while the average duration of pyrexia is one third less.

It may be objected that it is unfair to compare the treatment of rheumatic fever by one method – the use of the various salicyl compounds, chiefly salicylate of soda – with the various methods included under the head of non-salicyl treatment. But it is evident that the sum of the various averages is obtained, and that no method of treatment can have been found preeminently good, as the treatment by salicyl compounds is now said to be, otherwise it would have been all but universally followed. The probability of the results being fair seems then not unwarrantably assumed. Further Dr. Owen's series of 29 cases included only those treated by full doses of alkali, the most usual mode in pre-salicyl days, and the results are not markedly better than those in the other series.

When the several results of the two series are compared the advantage very clearly belongs to the salicyl method. Thus, first comparing the duration of pyrexia, the range in the non-salicyl set is nearly twice as high as that of the salicyl. The lowest average in the range of duration of pain under non-salicyl treatment is more than double that under salicyl, while the highest (seven in the next

loc. cit.

loc. cit. Lancet II/89, p. 1080

loc. cit. Lancet I/82, p. 9,54. Lancet II/82, p. 138

loc. cit.

favourable aspect is greater by 2·25 days.

Taking Dr Foggi's and Dr Wood's figures, the percentage of cases losing pain and becoming free from pyrexia in five days or less was under salicyl treatment nearly 50, under non-salicyl 16·3 – a very striking difference.

It must also be noted that under the treatment by salicin etc. the pain is often more quickly relieved than the figures might indicate – these figures representing the length of time before cessation of pain. In the majority of cases in both series pain appears to have been relieved before pyrexia ceased.

A very important question is the liability to relapse. In this respect the individual tables reveal curious differences. Under salicyl treatment relapses occurred in from 16·6 to 35·3 per cent of the whole number of cases. The individual percentages are Foggi's 26·2, Worm's 35·6, Crum 47, Wood's 15·8, Copeland's 35·3, Broadbent's 16·6. In the series of cases treated by other methods the range is from 5·4 to 27·6 – Worm's 14·9, Crum's 27·6, Wood's 5·4. In my own short series relapse was present in 50 percent of the cases. There would thus appear to be greater liability to relapse after treatment by salicyl compounds.

On examining the tables more closely I find that a very large number of those who became quickly free from

loc. cit.

Lamert I/92, Anm. 56, 134, + 138

pain and pyrexia relapsed. Three of 180 cases in which relief was obtained by fifth day (Hagge) are less than 9% had relapse, and 2% of these had more than one. In Dr Hood's series, of those who were relieved by the seventh day 45% had relapse. Of Dr Copeland's cases (82 in number) 61 obtained relief by fifth day as regards pyrexia and of these 21 had relapse of pyrexia. In 3 cases, in my own set of 14, relieved by the fifth day there was relapse.

Turning to the cases treated by other methods I find that in Dr Hood's series 8 out of 19 cases in which relapse occurred had been relieved by the seventh day.

Dr Copeland mentions that, though the greater number of patients who relapsed had ceased taking salicyl compounds, a considerable minority were taking as much as 60 grs. of salicylate of soda per diem. In two of my own cases the patient was taking salicin at the time of the occurrence of the relapse, while in another case, in which there were two relapses, the patient had stopped taking salicin on the same day. On the other hand several patients who had relapse were undergoing treatment by alkalis.

It has been suggested that the larger number of relapses under salicyl treatment is due to diminution of care on account of the early relief from acute symptoms. This seems borne out by the figures quoted above, which show that more

Laurent II/91, fr. 1031

" fr. 1120

than half the relapses under the treatment by salicyl compounds are found amongst those patients who obtained speedy relief. That this is not the full reason seems likely from the fact that considerably more than half (11 out of 19) of those who had relapse under other treatment were later than the seventh day in getting relief from pain + pyrexia. In my own set of cases 4 out of 9 (who had relapse) were not fully relieved until after the ninth day.

Dr Fagge makes a statement that patients are now kept longer in bed and on low diet than formerly, which is directly opposed to the opinion quoted on the previous page.

As regards length of stay, the range in five series, including 715 cases treated by salicyl compounds, is 23 to 36 days, while in three series, including 432 cases treated by other methods, the range is 26 to 36·2 days. This comparative statement is slightly in favour of treatment by salicyl compounds, but Dr Hood says that the average stay of the cases so treated is "perceptibly longer" than that of those treated otherwise. Probably the difference is not great.

If from the average length of stay the average duration of pain + pyrexia be deducted there is obtained what may be called the average period of convalescence. In Dr Warner's salicyl series this period was 29·4 days, in his non-salicyl series 22·4 days; in Dr Owens 19·25 and 19 days; in Dr

Lancet II/81, p. 1032

" p. 1120

(Art. "Rheumatism" in Quain's "Dictionary)

"On Disease in Children" p. 164.

Wells 26·25 and 24 days respectively. In Dr Copeland's series of cases treated by salicylate of soda length of convalescence averaged 31·4 days.

Keeping in mind the greater frequency of relapse under salicyl treatment it is evident that the longer period of convalescence is largely due to this frequency. In Dr Copeland's series the average duration of convalescence of 21 cases, in which pains paroxysms were absent by the 6th day and in which no relapse occurred, was 19·5 days, of 4 similar cases, in which relapse did occur, the average duration was 33·75 days. In 5 of my own series, in which no relapse occurred, average was 19 days.

Dr. Hilton Fagge says that after treatment by salicylic compounds patients "are left exhausted and pallid so that they slowly regain health and strength." This statement is corroborated by Dr Wood. Dr Mitchell Bruce says "anaemia appears to be more marked after treatment with salicylates" than under the older methods. On the other hand Dr Eustace Smith says alkaline treatment "encourages the tendency to anaemia"

Both under treatment by the salicyl and other methods there seems to be a large proportion of cases practically unaffected by treatment, unless perhaps the symptoms are prevented from becoming more severe, for I find that out

Werner – loc. cit.

of 350 cases treated by salicyl compounds there were 70 (or 20 per cent) in which pain & pyrexia lasted from 14 to 34 days or longer, while of those treated by other methods (also 350 in number) there were 149 (or 42 per cent). Under expectant treatment the duration of acute symptoms has been estimated at 9 days.

From a comparison of the evidence as put forward it would appear that under treatment by salicyl compounds, as usually employed, pain and pyrexia last for much shorter periods than when other treatment is employed; duration of convalescence and length of stay are not less; and frequency of relapse is greater. The number of cases which seem practically unaffected by treatment, i.e. as regards pain & pyrexia, is very much less under salicyl treatment. Not improbably there is greater debility induced by this treatment.

Considerable differences are found as regards the dose given. Thus in Dr. Taaffe's cases amount given in 24 hours varied from 60 grs to 150 grs. and upwards, in Dr. Burne's from 120 to 180 grs. and upwards, in Dr. Hall's from 90 to 180 grs.[2] In Dr. Copeland's cases the amount given was only once as high as 160 grs. in 24 hours, the dose being generally 15 grs. every 4 or 6 hours. In my own series the dose was at first 20 grs. of salicin every 2 or 3 hours. In the London cases the drug

Lancet II/81, p. 1091

employed was almost constantly salicylate of soda.

Dr Brunn remarks on the practical similarity of results though cases were dissimilar. Dr Copeland's results are on the whole better than Dr Hall's though the cases appear to have been very similar. This agrees very well with the statement previously made in regard to my own series.

So far all the evidence brought forward has been founded on statistics from hospital practice. The only statistical account of cases treated in private practice which I have seen is that of the late Dr C. L. Clemetson, of Gunnersbury, to be found in his Thesis for the degree of M.D. in the University of Edinburgh, which was published in the "Practitioner" (XXVIII, pp 321 sqq, + 401 sqq).

It is natural to expect that results should be more favourable when the cases occur in private practice, because the disease is seen at an early stage (in Dr Clemetson's series-19 cases seen on first day, 2 on second day, 3 on third day) patients are generally in better social circumstances, and there is no aggravation of symptoms such as is liable to be produced by removal to hospital. Dr Clemetson's figures bear out the correctness of this expectation.

His Thesis is based on a comparison of the results of treatment of 27 attacks in 23 patients. The average duration of pain he found to be 3·22 days, or if one case

were omitted 2·76 days. 23 (85·2 per cent) lost pain within 5 days – compared with 50 per cent in the case of hospital patients

The average duration of pyrexia was (in 22 cases) 3·3 days. The average both of pain and of pyrexia is lower than the lowest hospital average. The longest duration of pyrexia was 8 days, of pain 10 days. None of Dr Clouston's cases can be said to have defied treatment

Ten cases had relapses, but in six the patient had returned to work. The attacks might therefore be considered fresh ones. Of the remaining 4 two of the patients had exposed themselves. Convalescence was rapid and satisfactory. Dr Clouston did not find anæmia produced.

The most important point yet remains to be considered, viz. the liability to cardiac complications. There are, no doubt, great difficulties in estimating the comparative value of different lines of treatment in regard to their respective effects on the heart complications. Dr Lawson, in his Lettsomian Lectures, states these difficulties very succinctly. He says that (1) a murmur may be indicative of endocarditis acquired "incidentally at any previous time;" (2) the endocardial mischief may have preceded the other signs, or the murmur may be the result

Laurel Hill, Va. 1855

of adynamia of the cardiac muscle only, (3) the patient may be discharged as free from endocardial disease, and yet it may afterwards develop, having been present merely in the first stage of smoldering unrecognizable on auscultation.

These objections appear pertinent to all lines of treatment. By taking large numbers a comparative estimate may ~~appear~~ be considered approximately correct. Indeed bearing in mind the greater precision, in these latter days, in estimating the true value of auscultatory signs, the disadvantage in a comparison would probably belong to the older methods of treatment.

In the Medical Society Dr. Gilbart Smith stated that out of 1727 cases (in several classic series) treated before the advent of the salicyl compounds 54 to 56 per cent had cardiac complication, while of 533 cases treated with salicyl compounds 69·4 had cardiac complications. It does not seem to me probable that the difference of 13 per cent could be seen chiefly due to the greater frequency of the presence of cardiac complication before the commencement of treatment. Part of the increase may perhaps be due to the greater prevalence of adynamia of the cardiac muscle as part of the general feebleness left after treatment by salicyl compounds.

Dr Hood's figures give substantially similar

loc cit

loc cit

loc cit

results. His series include subjects of previous attacks as those of Dr Gilbart-Smith apparently do. Those of 350 cases treated by salicyl compounds the percentage of cardiac complications is 69·7, of 850 cases treated otherwise 59·8. Warner (excluding, as far as possible, old cases) says that cardiac complications developed in cases treated with salicylate of soda in 13·6 per cent, in cases treated by other methods in 14·2 per cent. In the table from which the latter percentage is taken I observe that there is one set of cases in which the number of heart complications is more than double that of any other year mentioned, the average duration of joint pains & pyrexia is double or more than double that of any other year, and the length of stay is much longer, but relapses are fewer. There is no similar exceptional set in the salicyl table.

It seems therefore fair to say that at least there is no difference in regard to liability to cardiac complication so far as Dr Warner's tables are concerned.

Dr Lawson states that pericarditis and endocarditis are shown by physical signs to arise and progress in patients who are fully under the salicin treatment. Dr Copland remarks that in his series the number of murmurs is "largely in excess of the number usually noted." "Heart affection may arise when a patient is

Stillé and Maisch "National Dispensatory" 3rd ed., p. 1[illegible]

"Theory & Practice of Medicine" 5th ed., p. 285

under them (i.e. salicylic acid and compounds) patient influenced. Dr. Frederick Roberts says that his belief is that alkalies are decidedly useful in preventing and relieving cardiac complications. In Dr. Clemston's series no cardiac complication arose while the patient was under treatment, and there were only two cases in which there was present recent cardiac complication when brought under notice.

Under treatment by salicin and its allies the greater frequency of relapse would seem to increase the liability to cardiac complications. Further, the short period of stay in cases of rapid recovery may allow of the patient going away with a heart affected with endocarditis yet in the stage unrecognisable by auscultation.

The sum of this matter would appear to be that salicyl compounds, as hitherto employed in hospital practice, have no greater, not improbably rather less, power of preventing or lessening cardiac complications than previously employed remedies.

In the face of the evidence adduced, especially the large proportion (20%) of cases which are practically unaffected by the treatment, it cannot be allowed that the salicyl compounds, as hitherto most largely employed, are the specific against rheumatic fever which they are sometimes said to be, e.g. by Dr. Mitchell Bruce in his

"Materia Medica and Therapeutics" p. 334. Even amongst Dr. Clouston's cases, treated under favourable circumstances, three cases (out of 27) were ill under treatment for from 6 to 8 days before temperature became normal, and in one case pain was present for 10 days. In one of my own cases after six days' treatment with salicin (20 grs. every 3rd hour at first, every 4th hour on fourth day) quinine was resorted to as an antiseptic. In two other cases temperature did not continue normal below 100° for 24 hours until the 14th day. Yet one of these patients had had 10 oz. of salicin.

I have been careful more than once to make a reservation in regard to the mode of carrying out the salicyl treatment, because the dose and frequency of repetition, as employed in the cases which have been under consideration in the series quoted, are widely different from those recommended by Dr Maclagan, to whom, as the originator of the treatment, some deference is due. The results brought forward in this thesis differ very materially from the glowing accounts given, in general terms only, in Dr Maclagan's work on rheumatism and elsewhere, and which of course only refer to his own line of treatment. He speaks thus: "In my own practice, I have come to regard a case of uncomplicated rheumatic fever in which pain is not quite gone, and the temperature normal, within 48 hours of the time

" Rheumatism, its Nature, &c., p. 14

Brit. Med. Journ. I/54, p. 713

" Rheumatism" p. 200

Brit. Med. Journ. II/54, p. 1124

that treatment commences, as an obstinate one".

In his own words his method of treatment is as follows: "Twenty to forty grains (of salicin) should be given every hour for six hours, or until pain is relieved (which is generally within that time), and the same dose should then be given every two hours until the pain is gone, and the temperature at or near normal (which is generally the case within 24 hours). After that the dose is given at widening intervals of three, four, and six hours, for two or twelve days." Elsewhere he says it takes about an ounce of salicin or salicylic acid to remove the acute symptoms. "That quantity should be taken within the first sixteen or twenty-four hours in doses of twenty to forty grains. A second ounce should be consumed in the next forty-eight hours."

Dr Clendon's method was to give an hourly dose of 10 or 12 grains of salicylate of soda "until pain was relieved or singing in ears came on", afterwards less frequently, then continued (or salicin given) for a few days three or four times a day. He says salicin must be given in doses of 15-30 grains.

Prof. Quinlan says he begins boldly with 30-60 grs. of salicin, according to the severity of the symptoms, every hour for three hours. If temperature be reduced at least one degree he continues for three hours more, when probably there will be a further fall of two or three degrees. If at the end of third hour of treatment the temperature is unaltered

"Rheumatismus" fm 200

Lamarck, I | 92, fm 9 + 54

Lamarck, II | 91, fm 1031

he adds two grains to each dose for two hours and again adds 1 grm. if necessary. These large doses do not cause any inconvenience.

I have already mentioned that Dr Owen found that there seemed no difference in result whether the dose given was larger or smaller. Clouston's dose is considerably less than either Macleyan's or Quinlan's.

The results mentioned particularly by Dr Clouston and in general terms by Prof Quinlan are much better than those quoted in the London debate and in my own series. (All Dr Macleyan's cases were probably in private practice - the majority of Quinlan's were in hospital.) If then, as appears likely, the amount of the dose is, within certain limits, of no great importance, it would seem that frequency of repetition is of considerable consequence.

Dr Macleyan says that the active compounds need to be given frequently because they are so rapidly eliminated. This is denied by Dr Copeland, because, he says toxic symptoms are frequently only produced after several doses, a cumulative effect being thus produced, and the reaction in urine with perchloride of iron may be present days after the administration of the drug has ceased. Dr Tapp mentions a case in which the reaction was present for eight days after administration had ceased.

If we consider on the one hand the marked relief

Lancet, I/82, p. 144

Brit. Med. Journ. I/82, p. 713
Lancet I/82, Br. Med. Soc. Address

of pain and the generally early apyrexia under the salicyl treatment, and on the other the smaller number of relapses, + the (not improbably) smaller liability to cardiac affection under other, very probably alkaline, treatment it is not unnatural that a combination of the two methods should suggest itself. On this point I may quote some pertinent remarks made by Dr Owen in the London debate. As regards heart affection being less frequent at St George's Hospital he suggests that this may be due to the practice of combining alkalis with salicylate being more frequent there than elsewhere. Dr Fuller and Dr Dickinson had shown that alkalies had great influence in preventing cardiac complication. It seems to me that if salicyl compounds benefit by their antipyretic action, alkalies may do so by their diuretic action.

Dr Maclagan strongly recommends salicin in preference to salicylate of soda as less liable to produce unpleasant effects. Besides he says that as salicin is a bitter tonic convalescence is more rapid. He quotes elsewhere reports from provincial hospitals, in many of which the presence of toxic symptoms after the administration of salicylate of soda is noted, while in some cases a preference for salicin is noted. Eight out of 54 cases treated with salicylate of soda had toxic symptoms (Hall). In my own experience in private practice most patients soon complain of ringing

Lancet, II/91, p. 1121

"Yearbook of Treatment, 1885, p. 76

Lancet, II/91, p. 1031

Brit. Med. Journ., II/84, p. 1124

in the ears. In Dr Copland's series toxic symptoms appeared in 28·5 per cent of the cases. Dr Fowler drew attention to the difference of results when salicylic acid prepared from wintergreen oil was used. Dr Dunlop uses only the natural alkaloid and gives the large doses above alluded to without toxic symptoms being induced. It is clear that at the present time salicylate of soda is largely preferred, notwithstanding the strong recommendations of Maclagan and a few others, for Dr Dyce Duckworth says that a firm of wholesale druggists lately told him that in the previous year they sold 4500 lbs of salicylate of soda and only 200 lbs of salicin.

Some physicians employ salicylate of soda at first and salicin afterwards. Dr Hilton Fagge says that he found this advantageous.

The use of fly blisters – applied to the precordial region – is an adjunct to the prevention treatment of cardiac complications. This is considered particularly valuable by Dr Dunlop, who had only 5 cases of cardiac complication in 102 cases of rheumatic fever (all but 23 being hospital cases). "In any case", he says, "in which the slightest sound of bruit or failure in the systolic sound of the heart is noted I am in the habit of applying a large fly blister over the whole cardiac region." The late Dr Herbert Davies found that out of 50 cases

Lancet I/82, p. 245

× Better put this parenthesis in a footnote & make it clear what it means by altering the words. As it stands it is not at all clear - "more manageable" — than what? and why?

of rheumatic fever, treated by blisters round every inflamed joint, there was none in which cardiac complications arose. Acute symptoms were also quickly relieved and relapses were infrequent. Possibly the cantharides may act otherwise than as a mere counter-irritant.

As the result of this critical analysis of the recent literature of the treatment of rheumatic fever the conclusion arrived at is that the only benefit, and it is not a small one, conferred by the introduction of the salicyl compounds as yet proved is the lessened period of pain & pyrexia. The evidence in regard to liability to cardiac complication, relapse, length of stay, and length of convalescence is at least quite as much against as in favour of treatment by these drugs.

In the present state of knowledge, then, my own line of treatment would be somewhat as follows: I would give 15 grain dose of salicylate of soda (because more manageable, less likely to be adulterated on account of the greater demand, and probably more efficacious with smaller dose) every hour until relief was obtained or toxic symptoms became pronounced, together with a full dose of alkalis (potass. bicarbonate and acetate) every 3rd hour. The salicylate (or salicin) would be

continued as the conditions of the case might demand. In the event of any suspicion arising in regard to the purity of the cardiac sounds I should apply a precordial blister (cantharides), provided there were no contra indications. This line of treatment is of course only provisional, because, in the absence of satisfactory pathological knowledge, it is at present impossible to frame a line of treatment which is likely to be universally suitable or nearly so. Besides, the individual methods of carrying out the salicyl treatment which have been quoted exhibit not a little diversity.

In conclusion I would suggest several questions as affording suitable material for further investigation.

(1) The most suitable dose? and the necessary frequency of repetition?

(2) Whether salicin ought to be preferred to salicylate of soda, or *vice versâ*?

(3) Whether, or not, there is a distinct advantage in combining the alkalin with the salicyl treatment?

(4) Whether any benefit is to be expected (from salicyl compounds) if purpura be declinate?

(5) How long, and in what dose, the drug requires to be continued? Also what regimen is necessary during convalescence?

(6) Whether in cases generally, as in my own series, patients who have had one or more previous attacks, are less quickly relieved, and more frequently relapse? Also, in what dose, and how long treatment ought to be continued in such cases?

(7) Whether precordial phyblisters are really preventive of cardiac complications?

Notes of Cases

M. M. - female - aged 13 years. Admitted 24th Oct, 1881. No previous attack. Began several days before admission. Many joints affected. Swelling slight. Temperature on night of admission - highest recorded - 102°F. V. S. (apex) murmur present when admitted. Ordered 20 grs. of salicin every 2 hours. Pains gone next day. Temp. not below 100° until 5th night. Went on satisfactorily until dismissed on Nov. 26th.

J. K. - female - aged 17 years. Admitted Nov. 24th, 1881. No family history of rheumatism. Patient had had two previous attacks. Joints not much swollen or red. Temperature on night of admission 99.8°. Temperature rose to 103° on night of 26th and pain became worse. V. S. murmur present on admission. Ordered on 28th 20 grs. of salicin every 3rd hour (previously 30 grs. potass. bicarb. & 10 grs. potass. iodid. every 4th hour). A. S. murmur noted on 28th. On 2nd December it is noted that pain is

slight, but temperature remains 103° at night, 102·4° in morning. On 4th quinine was given to reduce temperature. Pain & fever reappeared on 19th Dec, when the patient was taking a quinine tonic. Dismissed Dec. 29th.

M. F. - female - aged 19 years. Admitted 29th Nov., 1881. No previous attack. Previous duration of attack one week. Joints somewhat swollen & red. No cardiac affection. Temperature on night of admission 102°. Temp. below 100° on 3rd day, when the pain was also relieved. Had 20 grs. salicin every 3 hours at first, every 6th hour on fourth day. Dismissed Dec. 12th.

T. S. - male - aged 16 years. Admitted 21st Feb., 1882. No previous attack. Had had pain more or less for about four weeks. Temperature 101·4°. V.d. murmur present on admission. Joints not markedly swollen or red. On morning of 2nd day temp. 99·4° and pain gone. Dismissed 21st March - murmur still present.

J. H. - male - aged 20 years. Admitted 7th January, 1882. No family history of rheumatism. Previous attack 2 years before. Present attack began a week before admission. Number of joints swollen, but not red. Temp 102·5°. Jan. 14th Pain less - Temp. lowest 101·8° - highest 104°. Jan. 15th Pain much less - Temp lowest 101°, highest 103·8°. Salicin has been given nearly all along in 20 gr. doses every 2 hours. Jan. 25th Temp both night & morning below 100°. Ordered alkaline tonic. Feb. 1st. Has albumen - temp 100°

Feb. 4th Removed to asylum. No cardiac lesion. This patient took in all 57½ lb of salicin.

C.B. – male – aged 54. Admitted 24th January, 1882. No family history of rheumatism obtainable. Previous attack 14 years before. Began week before admission. Several joints affected. Temp 103°. Jan. 25th Temperature quite normal – pain all but gone. Salicin (20grs.) 5iiss at first every hour for two hours, then every two hours. Precordial blister was applied on first day on account of 1st sound appearing rough. Jan 31st Ten grains potass. iod. thrice daily. Feb. 14th Pain much worse, Temp 101·2–104°. Salicin every 3 or 4 hours. Blister. 19th Temp reduced. Dismissed April 14th. Pain showed tendency to remain in one or more joints.

S.A. – male – aged 36 years. Admitted 24th May, 1881. No family history. No previous attack. Previous duration one week. No cardiac affection. Temp 103° at night. 5iss salicin (20grs.) every 2 hours. 28th Temp at night now 99·6°. 30th Pain almost gone. Salicin every 4 hours. June 2nd Pain in left shoulder – chronic – without rise of temperature. Had also lupus. Dismissed July 12th.

A.M. – male – aged 42 years. Admitted 7th July, 1881. No definite family history. No previous attack. Previous duration two weeks. Some swelling of knees. Temp 101·6°. 5iss salicin (20grs) every 3rd hour. 9th Pain gone since yesterday afternoon. 10th Temperature normal. No risk of cardiac complications. Dismissed 30th July.

G.C. – male – aged 37 years. Admitted July 5th, 1881. No family history. Previous attack 12 years ago. Illness began 6 days before admission. Many joints affected. Temp. 101·6°. Salicin (20 grs.) every 3 hours. 14th Pain nearly gone. Distinct murmur. 17th Temp. below 100°. 22nd Temp. 101·6 – no return of pain. Patient ~~ordered~~ had iron ordered potass. iod. (gr. 10) every 6 hours. Second relapse of temperature & pain on 30th. On both occasions salicin was stopped the same day. Dismissed Sept. 14th.

W.H. – male – aged 21 years. Admitted Aug. 10th, 1881. No family history. No previous attack. Present attack of 10 days duration. Several joints affected. Temp. 101°. Salicin (gr. 20) every 3 hours – blisters to painful joints and precordium. No valvular lesion. 15th Temp. below 100°. 20th Salicin discontinued. 23rd Temp. 101°, but presence of pain not specially noted. Sept. 10th Return of pain – temp. 100° at nights. Had alkalies after salicin.

E.K. – female – aged 19 years. No family history. Admitted 4th March, 1882. Indefinite history of pains on previous occasion. Attack of four days' duration. Several joints swollen and. Temp. 102·6°. 5th Pain quite gone. 6th Temp. 99°. No cardiac lesion. Given 20 grs. salicin every 2 hours at first. Dismissed 21st March, 1882.

P.M. – male – aged 22 years. Admitted 4th March, 1882. No family history. No previous attack. Present attack of 5 days' duration. Cardiac murmur on admission. Ordered salicin (gr. 20) every 2 hours and a precordial blister. 13th Pain again much worse. Temp. still 102°. 17th Ordered alkaline mixture. 24th Temp. still 101° at night.

31st Pain gone. Apr 2nd Temp below 100° throughout 24 hours. Dismissed 21st April, 1882

Jelp - male - aged 38 years. Admitted 17th March, 1882. No family history. Previous attack 13 years before. Present of a week's duration. Not much swelling. Cardiac murmur. Temp 101·6°. Salicin every 2 hours in 20 gr doses. 20th Pain much less. 22nd Temp below 100°. 28th Return of pain. Temp 100°. Apr 6 Pain gone & temp normal. Dismissed 22nd April.

Whitt - male - aged 39 years. Admitted 21st March, 1882. Mother rheumatic. Previous attack 2 years before. Present attack of nine days' duration. Temp 101·6°. Salicin (gr 20) every 2 hours. 23rd Pain gone. Temp 102·8°. 24th Salicin thrice daily. Apr 4th Temp has for first time been below 100° for 24 hours. Apr 21st Relapse of pain - temp not noted. Had been ordered before this relapse an alkaline & iron mixture. Dismissed May 4th, 1882.