The majority of cases recover of themselves; and, as regards their treatment, probably the less of it the better. These cases are cases whose temperatures fluctuate daily between 103° and 104°, rarely remaining any long time at the latter point; and to give them specific treatment is useless, for they recover of themselves, and are, in my opinion, best left alone. The remainder which die, are cases in which the prominent feature is cardiac weakness, cases whose temperatures fluctuate between 104°, 105°, and upwards; or cases with very low temperatures and extreme depression of the nervous system, due to some peculiar effect of the disease.

These are the cases for which treatment is needed; but I imagine it would occur to no one to give such cases—cases which cannot even be “changed” without suffering from exhaustion—a cold bath every two hours. Liebermeister expressly says that “a very high degree of heart-weakness is an important contraindication;” and, further, that many patients do not bear a very frequent use of the bath. Hence, taking together the cases in which the cold bath treatment is inadmissible from cardiac weakness, and the cases which do not bear it, we exclude from its operation all the cases in which it is desirable that active treatment should be used. The cold bath treatment, on the showing of its own supporters, then falls to the ground.

The treatment which we have been considering attracted attention by reason of the very favourable results which were said to be obtained by it. In some cases, the mortality was said to have been reduced to 3 or 4 per cent.; and, more recently, to nothing. Admitting that relapsing fever, the normal mortality of which is about 3 or 4 per cent., that the “typhus” of young people whose normal mortality is very low; that all febriculae, in which the mortality is nothing, were excluded; and, finally, that the enteric was enteric as we know it in London—points on which, by reason of the loose way in which the term “typhus” in Germany is applied to diseases perfectly distinct, I entertain grave doubts—I should still prefer, judging from my experience, to believe that nature of cases, not treatment, determined the favourable results referred to.

Whilst, however, I do not believe in the systematic and routine employment of the cold bath in enteric or any other fever, I do not say that it is of no use at all. On the contrary, as a means of cleanliness and comfort, it will be useful in the milder cases; it will sometimes relieve restlessness, and occasionally promote sleep; and I would not deny that, judiciously given, it might occasionally determine the change to recovery. In a word, largely varied to suit individual cases, it is an useful help in the treatment of enteric fever; but to say this is one thing, and to say that it has abolished death is quite another.

ON THE ANTIPYRETIC ACTION OF SALICIN AND OF THE SALICYLATES; ALSO OF KAIRIN.

Read in the Section of Pharmacology and Therapeutics at the Fifty-Second Annual Meeting of the British Medical Association.

By F. J. B. QUINLAN, M.D. Dubl., F.R.C.S.,

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FROM the earliest ages of medicine, increased bodily heat has been recognised as the essential concomitant of the febrile condition; and its observation, even by the unaided sense of touch, has been employed as one of the most reliable modes of gauging the progress of fever, and of determining the effects of treatment. The use of instruments of precision for the estimation of the bodily temperature has given exactitude to what was previously only an approximation; and, with the aid of the clinical thermometer, we follow the rise and fall of the thermic wave with complete accuracy. This is particularly shown in the action of salicine, and of the salicylates in rheumatic fever; and it is in reference to this that I propose to consider them; for, although possessing a certain antipyretic power in pneumonia and in febrile diseases generally, they cannot be compared to quinine in this regard. Their action in rheumatic fever must be a satisfaction to every practitioner, for it would not be too much to say that they have removed this formidable malady from the list of *opprobria medicince*. In a celebrated discussion, held about a quarter of a century ago, an eminent physician expressed his belief that the only certain remedy for rheumatic fever was “patience, flannel, and six weeks,” and he would doubtless now be surprised to see the most formidable cases mastered in less than as many days; and this is to be accomplished by the free and frequent use of the sodium-salicylate, or, much better, of the natural alkaloid salicin itself. This latter I now altogether employ.

I have given up salicylic acid, on account of its sparing solubility; and if its sodium-salt be used in the large doses which are necessary to prompt and complete antipyretic effects, the most unpleasant results are liable to arise.

In Bartholow's *Materia Medica* (1882, p. 528), the dose of salicin is given at from 10 to 30 grains, and of the salicylate from 15 grains to a drachm. Dr. Mitchell Bruce, in his *Handbook* (1884, p. 332), recommends from 5 to 30 grains of salicin, and from 10 to 30 of salicylate; while Dr. Whitla, in the last edition of his admirable work (1884, p. 420), speaks of 15 grains of salicylate every two hours for 3, 4, or 6 doses, and this is undoubtedly a safe and useful line of treatment as far as it goes. Dr. MacLagan, in his work on *Rheumatism* (1881, p. 200), recommends from 20 to 40 grains of salicin or of salicylic acid, at first every hour, and subsequently at more distant intervals, according as the symptoms begin to subside.

From a very extensive experience, both of the natural alkaloid and of the artificial phenol derivative, it appears to me that there is no use in giving either in doses of 15 grains every third hour, and that the proper treatment of rheumatic fever is, having carefully noted the temperature, to begin boldly with from 30 to 50 grains of salicin, according to the severity of the symptoms, and to twice renew this dose at hourly intervals. If, at the end of three hours, the temperature be found reduced by at least one degree Fahrenheit, the dose may be persevered in for three hours more, when a reduction of from two to three degrees Fahrenheit will probably be found, with a corresponding improvement of symptoms.

If, on the contrary, at the end of the third hour the temperature should be found unaltered, or even increased, an addition of 10 grains should be made, and persevered in for two hours, at the end of which another 10 grains should be added if necessary; and, unless in some very exceptional case, the struggle must and will end in the victory of the alkaloid, and that without the slightest unpleasant symptom. I have several times given 50, or even 60, grains every hour, but this is seldom necessary. When I began early last year with these heroic doses, it was suggested to me that there might be a risk; and I accordingly proceeded to test what was the largest dose that could be borne without inconvenience.

Catherine C., aged 42, an averagely strong adult, was convalescent from acute rheumatism. She was up every afternoon, and was taking 30 grains of salicin daily, to prevent the relapse which is liable to occur if the drug be abruptly abandoned. On March 14th of last year, I commenced a daily increase of five grains; and on March 24th, she took an eighty-grain dose of salicin, and continued it four days without any apparent inconvenience. This experiment was interesting at the time; but I have since given healthy patients, who were not on a course of salicin, as much as 120 grains at a time, without any apparent result.

It has been asserted that cases of rheumatic fever treated by salicin, or by the salicylates, are more liable to cardiac metastatic troubles; but this is entirely contrary to my experience of 102 cases so treated, in which there were only five cardiac cases. One of these, Margaret D., aged 23, terminated fatally; but for this there were circumstances fully accounting. The other four made perfect recoveries; one of them, Henry McD., a cabdriver, aged 27, being of very great severity and persistency; and, in his case, it may be remarked that the salicin for the rheumatism, and the grey powder for the endo- and pericarditis, were given together. In any case in which there is the slightest want of tone or fullness in the systolic sound of the heart, I am in the habit of applying a large fly-blister over the whole cardiac region; and this I regard as a most important adjuvant to treatment, and a prevention to cardiac complication. Salicin is best taken on the empty stomach; and the handiest mode of administering it is either a capsule or wafer-paper. Suspended in milk, it is easily swallowed. Dr. MacLagan has remarked its tonic after-effects during convalescence; and this I can fully confirm.

No practical physician will for a moment doubt the antipyretic powers of salicylic acid, or of its more handy and soluble sodium-salt, in the treatment of acute rheumatism. To promptly master this disease, however, they must be given in hourly doses of from twenty to fifty grains; and I have seldom so employed them without producing nausea, vomiting, general depression, drumming of the ears, and, occasionally, temporary interference with sight or hearing. It is difficult to account physiologically for the marked difference in the clinical action of salicine and of the salicylates; and if we admit the hypothesis, generally received at present, that salicin is converted, in the system, into salicylic acid, the difficulty is proportionately increased. I see many objections to this view; and, without advancing any speculative opinion on an obscure point of therapeutical chemistry, would suggest the consideration whether both salicin and the salicy-

lates are not converted into salicyl. There is yet another possibility of accounting for the sickening and depressing effects occasionally produced by the salicylates, namely, that the acid made from carbolic acid is sometimes impure. Salicin, in latter years at least, is almost invariably a pure product. Reviewing the whole subject, I decidedly lean to the use of salicin in preference to any of the salicylates. It will do all that they can do; it will do so more effectually, and without any ill effects; and, lastly, the dose of salicin is practically unlimited.

Kairin-hydrochlorate, the hydrochlorate of oxychinolin-ethyl, another phenol derivative, was introduced to the profession, about two years ago (*Berlin. Klin. Woch.*, 1882, 1883) by Dr. Filehne, and appears to have a future before it. My experience of it is limited to four moderate cases of rheumatic fever, in which I found it a reliable, harmless and satisfactory antipyretic. It is a yellowish grey crystalline powder, very soluble and manageable, but with an intensely acid burning taste. It is best given in wafer-paper, and should be always followed by a drink either of water, or, better, of warm weak tea. I gave it in doses of ten grains every hour and a half; and found that, after about four doses, the temperature was reduced, the pulse lowered in volume, and copious perspiration brought on. The coloration produced in the urine was a slight greenish yellow. I took two doses of it myself, but without any apparent effect. It has been taken in doses as large as one and a-half grammes.

Guttmann has used it (*Berlin. Klin. Woch.*, July 30th, 1883; *London Medical Record*, November 15th, 1883) in forty-two febrile cases, including pneumonia, measles, phthisis, typhus, scarlatina, pleurisy, peritonitis, erysipelas, ague, and septicæmia. He gave hourly doses of from half a gramme to a gramme throughout the whole day. In three or four hours the temperature fell to normal, but soon rose again as the effects passed off. Perspiration was induced, along with diminution of the force and frequency of the pulse. The urine was green or black for thirty-six hours. This effect of the kairin subsided rapidly, leaving the disease unaltered.

Erlanger (*L'Union Médical*, October 4th, 1883) recommends the sulphate of kairin, a yellowish brown powder, easily soluble, of a salty taste, and of an aromatic odour. A single dose of three decigrammes has no effect upon the temperature; but half a gramme to a gramme will cause a fall of from 2.5° to 4° Fahr. This effect appears in twenty minutes, and lasts two hours with half a gramme, and three hours with the gramme-dose. Repeated doses cause a rapid fall of temperature.

In pneumonia, the relief supervening upon the fall of temperature is stated to be very marked. The temperature can be kept normal by the administration of three-quarters of a gramme every two hours. If this quantity be exceeded in elderly or delicate persons, cyanotic effects are said to be produced. A curious inconvenience (*Revue des Sciences Médicales*, October 1883) sometimes attending the use of kairine is a pain in the nose, radiating into the frontal sinuses. Professor Veraglia ("Nota sulla Kairina," *Gaz. delle Cliniche*, vol. xix, 24, 25) states that this itching sometimes amounts to pain; he has also noticed a dryness of the fauces, resembling that produced by atropine.

My own experience of kairin being limited, I have endeavoured to present a few reliable quotations of its effects. I think it is a good and safe antipyretic; and that, when its action is better understood, it will prove a valuable addition to the therapeutic armory.

Professor GAIRDNER (Glasgow) said he had been invited to appear in the present discussion, and he was rather glad of the opportunity of appearing, because it would enable him to introduce into the discussion, and perhaps to qualify somewhat, as the result of further consideration, certain statements which, when made years ago, had been considered, by some, unduly conservative. Some years ago he made a kind of protest against the extravagant terms in which the use of the cold bath, and very strong drugs also, were advocated as antipyretics, especially in a well known article on the treatment of typhoid fever in Germany. They might or might not say that he had gone too far, but he wished them to have a clear conception of what brought about that revolt in his mind. He was brought into the practice of medicine just at a time when people were becoming distrustful of those extremely active methods of their forefathers, when doubt was being thrown upon the efficacy of blood-letting, antimony, and mercury pushed in heavy doses, which were formerly considered indispensable; and he must say that his mind not only shared those doubts, but was carried by them, perhaps, into scepticism, to a considerable extent, in regard to other remedies then in vogue. He believed that much mischief had been worked by strong drugs, and it required the extreme, and, in its turn utterly unreasonable, rebuff—almost amounting to a kind of slap in

the face—from homeopathy, to cure the profession at large of these old and bad practices. Then came a new phase; and stimulants—the very antipodes, as it was supposed, of the older methods—were lauded, and given in all diseases, not merely because debility was then actually present, such as to require stimulation, but in anticipation of debility. In typhus fever, it was said that it was absolutely necessary to give strong stimulants in high doses early, in order to forestall the debility. The effect of all that upon his mind was a reaction against this dangerous tampering with the human organisation with strong agencies; and, accordingly, he had been compelled, as it were, to engage in a series of carefully watched experiments on stimulation, extending over years, as regards typhus fever in particular, the result of which was, that in the *Lancet*, in 1864, and in other papers extending down to 1871, he had been able to show pretty satisfactorily, that these huge doses of stimulants were not only unnecessary, but were extremely injurious, and that the treatment of typhus fever, and of other acute diseases, might be conducted much more successfully with very small doses of stimulants. As a matter of actual experience, he had accustomed himself to the idea that typhus fever, judiciously treated in hospitals, might, under favourable circumstances, be managed so as not to have a mortality of more than 9 per cent.—that is, in cases at all ages and in both sexes, as they occurred. He said nothing of his own experience, which was on a smaller scale; but Dr. Russell's experience in Glasgow, in many thousands of cases accurately watched before 1871, had reduced the mortality of typhus fever by simple common sense, and by careful management of details of dietetics, and comparative abstinence from high doses of stimulants, to about 9 per cent.; and day after day it was found that the using of stimulants in large quantities, or drugs in large quantities, tended to an increase of mortality and of bad symptoms. As regarded typhoid fever, which was the disease now in question—in regard to the masses of statistics turned out in Germany claiming for the cold bath an enormous reduction of mortality—he had simply to say that in Germany the mortality of typhoid fever started from a point enormously greater than anything to which we had been accustomed in Glasgow or Edinburgh hospitals. The normal mortality in Germany, before this interference of the cold bath treatment, was even stated at 25 or 30 per cent. We started from a better condition; and the Germans were not at liberty to argue that the whole of the reduction was due to the antipyretic treatment. A large amount of it was due to the fact that the Germans had, through the cold bath and antipyretics, superseded much worse—that is, actively worse—methods of treatment. Moreover, he argued to himself, if typhus fever could be treated with an average mortality of 9 per cent., and typhoid with a proportion of deaths varying according to season, and other causes unknown, from 5 or 6 per cent. to 13 or 14 per cent. (which were the limits of variation in Glasgow hospitals)—if this were true without the use of antipyretics in the modern sense of the word, then it could not be true that these antipyretics were absolutely necessary to reduce the mortality to something like the same level in Germany to which it could be brought without the antipyretics in Glasgow. Such being the state of the facts at the time referred to, he (Dr. Gairdner) did not oppose, or wish to be considered as opposing, the careful and judicious use of antipyretics, or of any other remedies. But when he read in a work of the highest authority, that typhoid fever could not be treated successfully without a system of constant interference, both by baths and by strong poisonous drugs, regulated and controlled only by the thermometer, he thought it was expedient to enter a protest, in the shape of what he had entitled "cautions." He could by no means admit that the one object of treatment in an acute disease was to keep down the temperature by hook or by crook. It was impossible to regard the human body in an acute disease as a mere mass of overheated tissues, or to suppose that, by merely cooling it down outside, one could restore health and function when otherwise fatally disabled. When it was said that one must absolutely cool down the patient till it became necessary to give him stimulants to set him up again, he thought that the limits of safety in antipyretic practice had probably been exceeded. When it was said that, failing the cold bath, it was necessary to give enormous and repeated doses of quinine; and, failing these, enormous and certainly dangerous doses of digitalis, aconite, and even veratrum, with the single object of getting down, and keeping down, the temperature, in diseases certainly admitting of fairly successful treatment without nearly so much interference, he confessed that he had thought that the practice of medicine was running in a wrong direction, that they were likely to have the story of the past repeated once more—a time of energetic and active practice (so called); that is, of extremely powerful, and in some cases dangerous and even poisonous, remedies, so advocated as to make them appear indispensable and to place them, as such, in the hands of every

one all over the country. A system of that kind was very likely to run into abuse, and he could not, as a teacher of medicine, countenance it without considerable reservations. He thought it would be admitted that the doubt in his mind was a just one. It might have led him to appear a little too conservative, but his mind did not always remain in that condition. His mind was open. He thought there was a good deal which might be said in favour of the use of the cold bath, but he had not even attempted to employ it on the large scale indicated by its strongest advocates, because he did not think that the British statistics of fever required to be amended so much; and, in the second place, he had imbibed distrust of strong routine-measures, which required to be kept under strict control. At the same time, he thought that a tolerably good case had been made out for the use of the cold bath early in the disease; and having read the results of the treatment in Germany, and more recently in Lyons, in London, and elsewhere, he confessed that his mind inclined to believe that a great deal of good might be done by the cold bath employed early in the fever, but he thought disappointment would accrue in the end if the cold bath were employed with any idea at all that it would make an entire revolution in their practice. It might be a good thing to use along with other things; but if medical men thought they were going to amend typhoid fever out of existence as a fatal disease, they would be disappointed. It was the best of the antipyretics, and the least subject to abuse. He thought the same principles applied still more to the rest of the antipyretics; quinine, when given with due regard to preserving the enfeebled digestive power, being the next best. Kairin he had only tried once. In considering such extremely disturbing remedies as digitalis and veratrum, his hesitation went on increasing; and he confessed he had no experience of any fever in which, merely in order to keep down temperature, it was advisable to run the risk of poisoning the patient; or even to say, as was affirmed, that it was of no consequence at all, if the patient became sick and vomited as the immediate result of the remedies given. His principle had been throughout to save up every atom of power and life; to save up everything as regards the enfeebled digestion and assimilation, thereby sustaining the strength of the patient. Any success he had had was due to a religious carrying out of that idea; and was he to be told it was of no consequence if the patient were put in a state of collapse, such that he must be revived again by stimulants, and so on? His mind revolted against that view, and was by no means to be entirely converted by such statistics as had been brought from Germany.

Dr. T. J. MACLAGAN (the President) had been a pupil of Professor Gairdner twenty-five years ago, and he could remember the extreme caution and care which Dr. Gairdner impressed upon his pupils. The subsequent long years of experience made the last speaker's words even more valuable.

Dr. ORD (London) was extremely glad to find himself in harmony with Dr. Collie. He had tried the use of the baths in hyperpyrexia in the treatment of fever, and in other cases where the temperature exceeded the limits of probable safety. The kind of bath which he had been in the habit of using was not quite the kind of bath to which reference had been made. It had been a less violent form. He used a bath into which the patient was immersed at a temperature of 90°, and, during the space of half an hour, the bath was cooled to 75°. That was a much milder medication; and he had to chronicle no obvious disadvantages from such treatment. As a beneficial result of the treatment, he had noticed that the temperature had been reduced in a remarkable way, but a number of symptoms had been produced in a more marked degree even than that recorded by Dr. Collie. He had noticed a diminution of delirium, headache, and the procuring of very long sleeps. In using this treatment in enteric fever, he had used it not as a routine remedy; he had considered himself by no means restricted from applying it to other diseases. He had used it in some cases of severe bronchitis, and in that he had found its beneficial influence illustrated more trenchantly. He would give an instance. It was that of a child suffering from bronchitis with a very high temperature. It was delirious, and apparently near death, from high temperature and difficulty of breathing. The father was a medical man; and, with his consent, he (Dr. Ord) put the child into a bath at a temperature of ninety-five degrees. When it had been immersed ten minutes, it fell asleep; its temperature fell, respiration was reduced to one-half, and the temperature, reduced eight degrees while the child was still asleep, when it was lifted out of the bath, remained in that state for three hours. After that it improved very much, and ultimately recovered. He had used the bath in a similar way in pneumonia and acute rheumatism, and Dr. Quinlan would forgive him for stating that it had succeeded in two cases in saving the patients where the salicylate had failed. He

used thirty grains of salicylate of soda every ten hours, and went on with half-hour doses. The patients had several hundred grains. The temperature was rising, and at the time of the bath there was a temperature of 106.7°, accompanied by delirium, timidity, etc., and he was inclined to suspect he had to deal with the evil effects of the salicylates. There was no subsequent rise of temperature with the use of the bath; however, in some way or other, by the combined action, the patients got well. Conditions of this kind had, for a long time, been making him think what was the meaning of fever. Dr. Collie had spoken of the futility of merely regarding the temperature in these cases. Dr. Collie was very right; but he did not say all he might. Dr. Ord then proceeded to comment on the cause of the rise of temperature, and to describe some investigations which he had made.

Dr. CURRIE (Lydney) spoke a few words on the subject of the action of kairin.

Dr. MACLAGAN also addressed the meeting.

Dr. QUINLAN, in reply, said that he would feel the greatest hesitation in differing with Professor Gairdner. He could not, however, avoid expressing his surprise that he should put cold baths at the head of the list of antipyretics and quinine next; and that he should not even mention salicin, which was, Dr. Quinlan thought, the most powerful antipyretic, as the one most free from risk. The case mentioned by Dr. Ord was in complete accordance with the views that he (Dr. Quinlan) had put forward. Dr. Ord administered the sodium-salicylate in legitimate doses, and it produced the effects which had caused Dr. Quinlan to give it up altogether, and that even in a more aggravated degree than usual. Under these circumstances, Dr. Ord most judiciously discontinued its use; but he did not use salicine in this case; had he done so, these serious effects would not have occurred. He believed that it would yet be shown that rheumatic fever was a germ-disease like intermittent fever; and that, like rheumatic fever, it was best combated by germicide remedies.

Professor GAIRDNER intimated that none of his remarks could refer to Dr. Quinlan directly, as he (Professor Gairdner) had not heard his paper.

Dr. COLLIE also replied briefly.

THE MICROCOCCUS OF PNEUMONIA.

Read in the Section of Physiology and Pathology at the Fifty-Second Annual Meeting of the British Medical Association.

By ROBERT MAGUIRE, M.D. LOND., M.R.C.P.,

Physician to the Manchester Southern Hospital; Pathologist to the Manchester Royal Infirmary; Assistant-Lecturer on Pathology in the Owens College.

I HAVE the honour of exhibiting to the members of the Section three preparations which illustrate the micrococcus of pneumonia, as recently described by Friedländer. One is a section of pneumonic lung; another a section of the kidney from a case of pneumonia; and the third is a preparation of the sputum from a similar case.

I may first say a few words as to the method which has been adopted in preparing these organisms. If a section of tissue be stained with methyl-blue, or with any of the reagents ordinarily used for detecting micrococci, it will be found that not only the micrococci, but also the nuclei of the cells, which are present, are stained by the colouring agent. In pneumonic lung, however, the exudation-cells are so numerous, that it is an exceedingly difficult task to discover amongst them, when stained in this way, any small and similarly stained micrococci.

The method used in preparing the specimens before you disposes of this difficulty in a most beautiful manner. It was introduced by Dr. Gram of Copenhagen, and a detailed account of it is found in the *Fortschritte der Medicin* of March 15th in this year. In the process, two prepared solutions are required: one is the gentian-violet-anilin-water solution used for staining tubercle-bacilli, and best prepared by Weigert's formula: anilin-water, 100 parts; concentrated alcoholic solution of gentian-violet, 11 parts; absolute alcohol, 10 parts. The other is a solution of iodine and iodide of potassium in water, in the proportion of iodine, 1 part; iodide of potassium, 2 parts; water, 300 parts. The section of tissue is placed in the gentian-violet solution for from one to three minutes, then in the iodine-solution for a similar time, and here a brown precipitate will be seen to occur. The section is then placed in absolute alcohol, until nearly all the violet colour is removed, and is afterwards transferred to oil of cloves, where a little more violet may be dissolved out. The section is finally mounted in Canada-balsam in the ordinary way. You then find, as is shown by the section before the meeting, that whatever micro-organisms are present are stained violet, but all the other parts are simply stained