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THE

SAFE DOSE OF THE SALICYLATES.

BY

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THE introduction of the salicylates into our pharmacopœia has proved satisfactory to the profession, to the credit of medicine, and of considerable benefit to the suffering patient. There are few of us who have not prescribed salicylic acid or its soda salt with very appreciable benefit, earning alike the gratitude of the patient, and the self-conscious satisfaction of having given relief, and not infrequently even cutting short the disease. These happy results have of late been somewhat clouded by the doubts that have been thrown by correspondents in our medical papers, and various annotations that have appeared in our medical press as to the occasional danger of the salicylates. At first the serious symptoms or toxic effects that were observed occasionally to follow the administration of this medicine were thought due to impurity in the manufacture of the drug, but

now after twelve or fifteen years of its very frequent prescribing there ought not, and neither do I think there is, any difficulty in procuring salicylic acid or the salicylate of soda free from any impurity or adulteration. It has occurred to me that the officinal dose of the British Pharmacopœia is too large, and ordered to be repeated too frequently, and I have thought, and perhaps with greater reason, that the undesirable and even occasionally alarming symptoms that have been noticed after its administration could scarcely have been due to the recognised dose of the salicylate prescribed. In February last I attempted to call attention, by a note published in the *Lancet*, to a case where 15 gr. doses of salicylate of soda were believed to have caused even a fatal result. As I received no reply, perhaps the readers of the *Lancet* thought as I did, that the death was in no way owing to the medicinal dose of the salicylates.

I wish to-night to consider what is a safe dose of this medicine, and also to ask your careful attention to two or three brief notes I will read to you, where the symptoms that followed the prescribing of the salicylates were serious and alarming, and especially, as to whether in your opinion the symptoms were, as was supposed, due to the salicylate of soda.

Allow me to remind you that the officinal dose of salicylate acid is 5·30 grs., B.P., '85; Martindale in his "Extra Pharmacopœia, '84, says 5·30 grs. *or more.*

Whitla in his work on "Pharmacy, Materia Medica, and Therapeutics," gives as the dose of salicylic acid, or salicylate of soda, 30 grs. in half an ounce of water every two hours, for 3, 4, or 6 doses, as the severity of the pain or height of the fever indicates; and adds subsequently, pain and fever will return if it be withheld, and yield again on its administration. Bruce, also, in the third edition of his work on "Therapeutics," p. 367, mentions 15 to 20 grs. as a moderate dose, and cautions that, as the pyrexia declines, the dose of the salicylate must be gradually reduced, as relapses are extremely common after it has been discontinued.

A year or two ago I attended a young lady for the hyperpyrexia of acute rheumatism. I quickly reduced her temperature from 107° to 104° by five or six doses of 20 grs. of salicylate of soda, given every three or four

hours, and subsequently to 102° by its continuance at longer intervals. I then at her urgent request discontinued it, as she said:—"I should now feel quite well if you would only leave out the medicine that you told me caused the buzzing in my ears and the fulness in my head." I complied with her request, and substituted for the salicylate an effervescing mixture of citrate of potash c ℥ v doses, vini colchici. On the evening of the second day, after the discontinuance of the salicylate, the hyperpyrexia somewhat suddenly returned, and was not again reduced even by a return to the scruple doses of salicylic acid or salicylate of soda. Death resulted from pericarditis in about twelve hours, consciousness being retained till within half an hour of death. (*a*)

Farquharson in his "Guide to Therapeutics," page 285, states 'that we may give salicylic acid in 20 gr. doses, repeated hourly for one or two successive days, and continued at shorter intervals if the disease resists forty-eight hours' medication."

Salicylic acid is one of those few medicines that acts specifically, and that we are able to predict with more or less confidence that it will reduce temperature, that it will ease pain of both joints and muscles when due to acute rheumatism, and that it will not infrequently cut short, and even cure, the disease for which it is prescribed. I am therefore desirous, and indeed anxious, that the apprehensions that have arisen with more or less cause as to its safety should be considered, and to know what is the safe dose, that the salicylates may be prescribed with confidence of happy results. With your permission I will now ask your kind attention to brief notes of two cases where serious symptoms were either caused or followed medicinal doses of the drug. One is recorded in the *Lancet*, of Dec. 18th, 1886, by Mr. Freeman, the other and more instructive was published in the *British Medical Journal*, of Feb. 5th, 1887, and the symptoms occurred in a patient an inmate of St. Mary's Hospital, and under the care of Sir Edwd. Sieveking. The case is recorded by Mr. Freeman as *a warning of the need of caution* in the use

(*a*) It was suggested in the discussion that this death was due to uræmia, but the urine had been tested, and was normal, and there never was any symptom of kidney mischief.

of salicylic acid, but the result appeared in no way owing to the dose of 15 grs., for only three doses were taken, and there had previously been cerebral symptoms. I cannot then believe that Mr. Freeman has here any sufficient reason to think, merely because the patient was comatose and the urine was albuminous, that the medicinal dose of the salicylic acid caused the fatal result. (*a*)

More important and more worthy of your attention is an interesting case of salicylic acid poisoning recorded in *British Medical Journal* of Feb. 5th, 1887, at St. Mary's Hospital, London, under the care of Sir Edward Sieveking. C. W., æt. 55, was admitted at 2.30 p.m. on Nov. 3rd, 1886. She had been treated by a medical man for subacute rheumatism, and had been ordered 15 grs. of salicylate of soda every four hours, but by a mistake on her part had been taking double doses of the salicylate mixture. The first dose was taken at 12 a.m., Nov. 2nd, and the last dose at 5 a.m. Nov. 3rd, and during this period of seventeen hours the patient had taken 120 grs. of salicylate of soda. On admission, the patient complained of a buzzing noise in the ears, some headache, and great deafness (she was naturally slightly deaf). The pupils were extremely contracted, the urine contained a large quantity of salicylic acid and albumen, about 1-10th of the latter depositing after boiling the urine with a little nitric acid. A saline purge was administered. Nov. 4th.—All the symptoms had considerably abated. The urine still contained a large quantity of salicylic acid, and a trace of albumen. Nov. 5th.—The urine contained a moderate amount of salicylic acid, but no albumen. Nov. 6th.—The urine was quite free from salicylic acid and albumen. The buzzing noise in the ears, the headache, and the extreme deafness had gone. The pupils had resumed their normal size. The patient was discharged a few days later quite well. *Remarks.*—The case is of interest as demonstrating the time taken for the elimination of the salicylic acid from the system.

As I read this, the symptoms of *poisoning* seemed of the slighest or at least insufficient to have apprehended a fatal result, but by some unaccountable mistake the

(*a*) For full account of this case *vide Lancet.*

dose had been doubled, but even *then it did not exceed the full officinal dose of* 30 *grs.* I would with all diffidence add, the symptoms, except the contracted pupils, appear to me to have been little more than the *physiological* and *not the toxic* effects of the salicylate. There is no coma, no insensibility; the patient describes her own symptoms: no difficulty of respiration, no alteration noticed in the colour of the urine, not even the olive-brown tint, as is occasionally seen when large doses have been given, nor the olive-green tinted urine that might point to the impurity in the manufacture of the drug. In the absence of these symptoms, as also of the graver toxic effects, such as delirium, visional hallucinations, dyspnœa, and cardiac failure after the primary excitation has passed off. I should upon less eminent authority have hesitated to have considered this case as one of salicylic poisoning. The patient recovered, and no antidote was given; had it occurred in my practice I think it would scarcely have crossed my mind that the patient was being poisoned by the dose she had taken, even double dose as it was. Of course I should have discontinued the salicylate or at least reduced the dose, and had I thought the effect that had been produced alarming or dangerous, I might perhaps have substituted salicine for the salicylate, which Prosser James mentions in his "Guide to the British Pharmacopœia." Dr. Maclagan has found "the cerebral symptoms produced by large doses of salicylic acid disappear on the administration of the salicin and withdrawal of the acid." Mr. George Robinson, in the *Lancet*, of October 2nd, 1886, mentions that he prescribed the salicylate of soda in a case of paraplegia, after only two doses of 15 grs., given at intervals of four hours, the patient complained of nausea, pain in the head, giddiness, buzzing in the ears, and faintness; he was, however, cautiously content to reduce the dose from 15 to grs. vij for four days, and subsequently increased to grs. x every four hours, with very decided benefit to the patient, relieving much the putrescence of the urine for which it was prescribed.

Gentlemen, it is necessary, as was forcibly demonstrated at our last meeting by Dr. Thudichum, that we should know the nature, strength, and properties, whether usual or unusual, of the medicines we prescribe,

that we may have confidence in the remedies we give or the relief or cure of our patients, and if any remedy be attended with risk of danger we must blot it out of our armarium medicinæ even if with a sigh of regret, for this is necessary for our tranquillity of mind, as well as incumbent upon us in our patient's interest and the public weal.

In conclusion, I ask for your experiences, the result of careful observations, if salicylic acid or its soda salt is a safe as well as effectual remedy, and in what dose, having due regard for the constitution of the patient and the disease for which it is prescribed, it may be ordered with safety; my own experience inclines me to think 10 or 15 grains of the salicylate of soda given at intervals of four hours is safe, and that there may have been perhaps needless alarm and apprehension as to the serious although not toxic symptoms not infrequently following this useful medicine.

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