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In 1764, Edmund Stone, a vicar in Chipping Norton, a small town in North Oxfordshire, England, reasoned that the bark of the common white willow tree (*Salix alba vulgaris*) might be a treatment for 'agues and intermitting disorders' (fevers):¹

'About six years ago, I accidentally tasted it, and was surprised by its extraordinary bitterness; which immediately raised me a suspicion of its having the properties of Peruvian bark. As this tree delights in a moist or wet soil, where agues chiefly abound, the general maxim, that many natural maladies carry their cures along with them, or that their remedies lie not far from their causes, was so very apposite to this particular case, that I could not help applying it; and that this might be the intention of Providence here, I must own had some little weight with me.'

In an account published in the *Philosophical Transactions of the Royal Society*, Stone reported that over the previous five years he had treated 50 cases of fever with willow bark, 'which never failed in the cure, except in a few autumnal and quartan agues'.¹

Edmund Stone's experience was not mentioned when more than a hundred years later, Thomas Maclagan, a doctor in Dundee, Scotland, reported on his use of salicin to treat the symptoms of rheumatic fever.² His reasoning was remarkably similar to Stone's:

'Rheumatic fever is now generally regarded as being produced by some cause or agency which is generated within the body. My own investigations into its pathology have led me to reject this view, and to adopt the old "miasmatic" view of its mode of origin, according to which the cause which gives rise to the disease is introduced into the system from without.'

Holding this view as to the pathology of rheumatic fever, impressed with the points of resemblance between it and intermittent fever, and bearing in mind that we have in quinine a potent

remedy against the latter, there seemed to me a good reason for indulging in the hope that some remedy would yet be discovered capable of exercising a similar, if not equally beneficial action on rheumatic fever.

... nature seeming to produce the remedy under the climatic conditions similar to those which give rise to the disease... it seemed to me that a remedy for that disease would most hopefully be looked for among those plants and trees whose favourite habitat presented conditions analogous to those under which the rheumatic miasma seemed most to prevail. A low-lying damp locality, with a cold, rather than warm, climate, gives the conditions under which rheumatic fever is most readily produced. On reflection, it seemed to me that plants whose haunts best corresponded to such a description were those belonging to the natural order Salicaceae, the various forms of willow.'

At the time that Maclagan suggested using salicin in rheumatic fever it had fallen into disuse and had even been dropped from the British Pharmacopoeia.³ We now know that this was a serious mistake, which raises questions about how salicin came to be abandoned. Maclagan's 1876 report of eight cases of rheumatic fever treated with salicin is an example of a treatment with effects so dramatic that carefully controlled research is unnecessary to infer confidently that they exist. As Maclagan writes, 'The sudden arrest of the painful symptoms, and the coincident rapid fall of pulse and temperature, followed so immediately on the administration of salicin that it is impossible not to attribute them to its use'.²

A subsequent *Lancet* report by a Dr Broadbent⁴ suggested that Maclagan had simply followed the practice and confirmed the results of German physicians Reiss and Stricker, who had assessed the effect of salicylic acid on rheumatic fever. This prompted Maclagan to note that his paper was about salicin, not salicylic acid, and that the results which he had obtained from the use of salicin were so remarkable that he had 'hesitated to publish

them till a sufficient number of cases lent certainty to them.' He went on to suggest that salicin had advantages over salicylic acid and claimed that 'those who try both remedies will not fail to find salicin the better of the two'.^{3,5}

These arguments among Europeans were put into perspective three months later when Maclagan wrote again to the *Lancet*, reproducing and commenting on a letter prompted by his original report, which had been sent to him from South Africa.⁶ On 14 April 1876, Frederick Ensor, Surgeon to the Provincial Hospital at Port Elizabeth, had written as follows:

'DEAR SIR – I have seen with much interest your papers in THE LANCET on the Treatment of Rheumatism by Salicin, and thought that the following story might be welcome.

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

The temperature in summer is very high, and the dryness of the atmosphere so great that surgical instruments or fire-arms never rust. The winter, with its clear bright sun and cool temperature, is most exhilarating. You can imagine that a doctor's life in such a region must indeed be a sinecure. On one occasion, however, I was sent for to visit the wife of a Dutch Boer, who was said to be very ill. I found my patient to be of the usual Dutch build, informe ingens, lying on a camp bed in a little tent, where the heat was something terrific; a naked bush child trying to fan away the cloud of flies, which was tormenting my poor patient, bound hand and foot, I may say every joint, in the cruel bonds of as fierce an attack of rheumatic fever as I ever saw. She was perspiring profusely. The time that has elapsed has obliterated my memory of pulse, temperature, and heart complication. I prescribed the usual alkaline mixture, with calomel and Dover's power at bedtime, and rode away.

Some two months after, my former patient entered my surgery, looking remarkably well, and I very naturally congratulated myself and her that she had recovered so completely. I was quite taken aback when she bluntly told me that my physic hadn't helped her a bit. On enquiring what had helped her, she said that the old Hottentot shepherd

had made her a decoction of the shoots of the willows which grow on the banks of the river, and that after taking this for a few days she began to get better.

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

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

Commenting on the information he had received from South Africa, Maclagan wrote:

'If what has already been published regarding the efficacy of salicin as a remedy for acute rheumatism should be confirmed by a more extended experience – as I have not the least doubt it will be, – it will form a curious commentary on our civilization, and on the advance of medical science, that one of the most common and painful diseases of the civilized world should have remained one of the approbria of medicine for many years after a remedy for it was known to the rude Hottentots of South Africa. Equally within the reach of both has ever been the means of cutting short the disease; but the untutored Hottentot shepherd used the proper means, while the accomplished European physician was trying this, that, and the other remedy, with results so unsatisfactory that he had almost given up the idea of ever being able to do more than watch the natural progress of the malady.

*I hope to receive more detailed information on the Hottentot practice.'*⁶

Maclagan does not appear to have pursued any further the 'Hottentot practice'. Indeed, a quarter of century later, a few years before his death, he still felt it necessary to defend his priority in using salicin in the treatment of acute rheumatism.³ He wrote: 'My observations on the treatment of acute rheumatism by salicin and the German observations on its treatment by salicylate of soda were independent and contemporaneous. If there is priority I claim it for my 1874 cases, which were undoubtedly the first cases of acute rheumatism treated with any of the salicyl compounds'.⁷

Presumably these civilized Europeans found it difficult to accept the possibility that the lowly Hottentot dwellers of the Cape of Good Hope, who were viewed as being at the bottom of The Great Chain of Being, may have been the first to discover

an effective treatment for the symptoms of acute rheumatic fever.

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