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## SALVARSAN AND OTHER REMEDIES IN OPHTHALMIC PRACTICE.

By FREELAND FERGUS, GLASGOW.

POSSIBLY in no region of medical science is it more difficult to estimate results accurately than in the very important domain of therapeutics. There are often so many factors that are quite unascertainable complicating the problem that it is difficult to estimate how far any drug is of use. Every now and again some remedy is loudly vaunted as being invaluable in certain forms of disease, but after a few years it passes out of notice and is no longer thought suitable for the very conditions for which it was regarded as a specific on its first introduction. That there has been material progress in therapeutic work must be generally admitted, but what real and lasting progress has been made in recent years has been almost entirely on the biological side, and probably we are only at the beginning of still greater advances in the same direction. When a remedy is at one time extolled as being of very special use under certain conditions, and a few years afterwards is rarely if ever mentioned, it suggests that the original introduction of that medicine was made without a thorough and impartial test. Possibly even in some cases it is boomed by manufacturers who have a financial interest in putting it on the market. One or two examples will illustrate our meaning. Some years ago certain organic preparations of silver were supposed to supersede everything else in the treatment of various forms of conjunctivitis. Three of the best known were protargol, argyrol, and collargol. The first was largely brought into notice by a book written by Dr. Darier of Paris and translated for the English public by Mr. Sydney Stephenson.



A more disappointing book we never read. It is absolutely destitute of any scientific information on the subject. It is a piece of mere empiricism and tolerably crude at that. How these remedies came to be popular and sold in the way they were, as germicides with important actions, is a mystery, for if there is one thing certain, it is that their germicidal actions are practically negligible. Many experiments have been made with strong solutions of these drugs. Cultures have been immersed in solutions of them for hours together and then sub-cultures have easily been obtained. It is difficult to believe that anybody can still hold that a few drops of a solution of any of these drugs introduced into the conjunctival sac for a few seconds can have any influence whatsoever on the flora of the conjunctiva. Undoubtedly they give better results than strong solutions of nitrate of silver, such as were at one time frequently used, for the simple reason that these preparations do no harm, which nitrate of silver unquestionably did. Looking back on the results of the treatment of gonorrheal ophthalmia with strong solutions of nitrate of silver, we cannot but think the result was in almost every case detrimental. The conjunctival sac was never sterilized although the protecting epithelium of the conjunctival membrane and sometimes that of the cornea were seriously damaged. The organic preparations already mentioned do no harm, nitrate of silver does, and hence these preparations appeared to the authors whom we have indicated as intrinsically of high value.

It has now been known for a considerable time that these drugs in the treatment of conjunctivitis are inert, and yet patients turn up in large numbers at our dispensaries and in our private clinics who produce letters from their medical advisers to say that they have been using protargol or argyrol for some weeks or months but without effect. Nobody who knows the facts of the case would expect anything else. Many years ago, indeed shortly after commencing the study of ophthalmology, I came to the conclusion that a conjunctivitis was the expression of one of two things, namely, either an uncorrected error of refraction or a microörganic infection. In the former case it is a question of measuring the error of refraction and correcting it accurately. In the latter it



is a matter of removing and not of killing the organism or organisms.

Another instance of a method of treatment which has been largely boomed was Röntgen ray and radium treatment for cancer. I do not suppose there is a single instance on record in which a case of cancer has been cured by these means, any more than there is on record a case of cancer which was cured by the Count Mattei blue or white electricities. It is possible, perhaps, that the employment of these remedies may give some relief in cases of inoperable cancer and may make the sufferer a little more comfortable, but evidence is totally lacking that treatment by radium or treatment by the Röntgen rays has ever cured cancer. Both of these remedies are becoming more and more placed on the shelf for that malady.

A third typical example is the difference between antiseptic and aseptic treatment. In the old days gauze dressings for wounds used to be thoroughly impregnated with carbolic acid. I myself have examined some of the discharges contained on these dressings and found them to be teeming with micro-organic life. Lister's application of Pasteur's great discovery, we venture to think, was the happiest that has ever been made in the science of medicine, but he did not realize that the means which he proposed for the destruction of germ life were not adequate for the purpose. It is no more wonderful that he did not see the whole of the ground which his work opened than that Isaac Newton saw the fallacies in the corpuscular theory of light, yet, as in the case of protargol, the old idea still persists.

We still find ophthalmic text-books figuring an undine and expatiating in the use of that instrument for applying boric solution as an antiseptic. That a special form of instrument should thus be widely advertised may be of use to the persons who have these appliances for sale. From our point of view it is probably the worst contrivance. You cannot kill germs, as far as we know, by anything which you can apply to the conjunctiva without destroying the membrane itself. You may remove the germs and thereby save the situation, but you will require a thoroughly good douche with a fall of at least eighteen inches and not less than a pint at a time to be used, and of all the apparatus for carrying out such a line of treatment



probably the undine is the least useful. When we find an instrument of that sort recommended, we cannot help suspecting that the author who advises it is still under the impression that the ingredients of the lotion are the important thing and not its method of application. With very few exceptions, the only useful element in any lotion is water which, if not to be painful, must be made isotonic with something or other, preferably with sodium chloride. We cannot help thinking that a man who prescribes boric lotion to be used in an undine has done very little observational work in conjunctival bacteriology.

There is, as is well known, the exceptional case of the use of zinc sulphate apparently freeing the conjunctival sac of the *Morax* parasite. No doubt similar instances of germicidal effects may be discovered, but apart from this, so far as we know, there is no other instance of an ordinary drug causing an infective microorganism to disappear so long as the remedy is applied only in such strengths as will do no harm to the conjunctival membrane. No one can foretell what the future may have in store, but that is pretty much how the matter stands at present.

But a very important question now arises. Of recent years the same country which gave us protargol and argyrol has given us a new remedy for syphilis for which the strongest claims have been made in influential quarters. It is said to be infinitely better than anything that has yet been used. Men specially trained are to be appointed by the State for its administration and no doubt a large section of the British public who are the victims of syphilis will have salvarsan or its substitutes administered to them.

The circumstance that certain practitioners are to be appointed for its administration points clearly to one thing, and that is that its administration is by no means free of danger, and indeed there is a very fair death-roll connected with the use of this drug already. The vital question thus comes to be: Is this treatment so overpoweringly superior to any other that we are justified in running the extra risk? Is salvarsan or neo-salvarsan so immeasurably superior to mercury that we are justified in running a moderate percentage of risk? If it were proved that these new drugs were an infallible remedy for



this terrible disease I would answer that question in the affirmative.

That however is very far from being the case; and in the state of doubt as regards this line of treatment in which I find myself I have ventured to record some cases to which I would, with all respect, call the attention of syphilologists. I am not one myself but have every confidence that those who are working in this particular department will ultimately get at the facts of the case. I see no more syphilis than is usually seen by ophthalmic surgeons in hospital and private practice.

To begin with, I found that salvarsan was a failure in interstitial keratitis. So far as that disease is concerned, mercury has given very much better results than these newer drugs. I believe that my experience is not singular in this respect. Other practitioners have also reported against their use in this particular disease. The explanation of this failure given by the advocates of this new line of treatment is that the cornea is a special tissue and that the drug does not reach it.

Now one thing is certain and it is that although in health there are no blood-vessels in the cornea still it contains a large number of lymphatics. The fluid which these contain is no doubt derived from the blood stream; why then should the drug not find its way into the tissue? I am at a loss to find an answer.

And here perhaps I may be allowed a short although, as it seems to me, an important digression. Recently I read a statement which in my opinion underestimated the gravity of interstitial keratitis. It was to the effect that the prognosis of this disease is favorable and that the cornea clears completely. Now my experience is that although in the main the prognosis is not bad yet I have never seen a cornea which was not to some extent damaged, and that permanently, by this form of keratitis. In some cases the injury may be slight, in others it is severe and materially interferes with vision.

My present purpose, however, is to call attention to five cases in which the organ of vision was involved by syphilitic disease otherwise than by keratitis and in all of which salvarsan or neo-salvarsan had been used. I shall make almost no comments but for the most part will simply record them as they occurred.



The first case is that of an officer who some six years ago consulted me for an acute iritis. He was put on mercury and atropine in the usual manner and the condition began steadily to improve. He had heard of the new treatment of syphilis and was anxious to try it as a permanent cure. I directed him to avail himself of the services of a colleague who is thoroughly authoritative in this line of practice. That gentleman was given a perfectly free hand and gave him what injections he thought proper. Thereafter a Wassermann reaction was taken and he was pronounced to be permanently cured of his disease, and all treatment was stopped. Ten months afterwards he re-appeared in my room, this time complaining of severe pains in his legs. I sent him to the same practitioner, who found that the Wassermann was now positive. He removed to another station and I cannot tell what became of him. I could not discover any definite ataxic symptoms, but at the back of my mind there was the idea that the pains in the legs might be the beginning of locomotor ataxy.

The second case which occurred about the same time is also very important. A patient came complaining of defective vision in the left eye. On examination I found it to be due to a slight optic neuritis. He admitted quite freely that he had syphilis. Like the patient whose case has just been narrated, he also had heard of the new treatment as a perfect and permanent cure of syphilis and was anxious to try it. I at once gave my consent and directed him to the practitioner who had administered the drug to the patient already mentioned. The injections were duly given and after a Wassermann reaction was found to be negative he was pronounced cured. Within six months he returned to see me and I found him suffering from an acute iritis which at once yielded to treatment with mercury. There had been no chance of a re-infection.

The third case is of special importance, for it suggests even more strongly than the first that instead of being beneficial neo-salvarsan had been injurious. The patient was a lad who, many years before the introduction of salvarsan treatment in any of its forms, acquired syphilis. When I saw him he had all the signs and symptoms of well-marked paralysis of the external rectus of the *right* eye. He was at once put upon mercury by the mouth and by inunctions and made a



thoroughly good recovery. A good number of years afterwards he heard of neo-salvarsan as a remedy which would entirely remove syphilis from his system. Naturally he consulted a practitioner who is justly much esteemed in this line of practice and the drug was duly administered to him. Two years afterwards he came to me complaining of complete blindness of the *left* eye. I found advanced optic nerve atrophy in the affected organ. He told me that he had not observed anything wrong with the eye before the administration of the drug, but that shortly thereafter he found the vision affected and that it had become gradually worse till complete blindness supervened. The administration of the drug may have had nothing to do with the onset of the atrophy, but in view of the facts which we know about soamin, which was previously supposed to be a perfect and safe cure for syphilis, the onset of the atrophy could not but raise suspicions.

The fourth case is one in which the patient had no fewer than eight injections. The first four were given in July and August, 1916, and the last in March and April, 1917. In August, 1917, he came to me complaining of diplopia, which I found to be due to complete paralysis of the internal rectus of the right eye. The movements upwards and downwards were also slightly restricted and there was slight dilatation of the right pupil. The visual acuteness of the eye was  $\frac{6}{12}$ . He had also all the symptoms of spinal sclerosis. It was quite evident that in this case the drug had not so relieved him of the protozoön as to prevent nerves hitherto unattacked becoming affected.

The first, third, and fourth cases help to strengthen the view that salvarsan, containing as it does arsenic, may be specially harmful to nerve tissue.

The fifth and last case also would seem to show that this method of treatment is not of permanent value. The patient received five injections in Sydney about the month of February, 1916. A Wassermann was done and he was pronounced to be perfectly free of the disease. In July of this year he was admitted to the Fourth Scottish General Hospital with an acute choroido-iritis of the left eye, and so authoritative an observer as Professor Muir pronounced the Wassermann to be again positive.

My experience of syphilis is small. One swallow does not



make summer, and five even such striking cases as the above do not entitle one to do more than hold his opinion in reserve, but that I certainly am doing. I would suggest, however, that all cases in which the drug has been used should be registered and followed up for some years. If the drug is more efficacious than mercury and more lasting in its results and does not cause any ulterior damage, then it may be justifiable to run a certain risk, but if not, then it should not be used. I have formed no dogmatic opinion and am prepared to consider carefully any well ascertained facts which may be stated by those who have a large practice amongst the unfortunate victims of this malady.

