

the cystoscope shows a bladder free from, or but slightly infected with, tubercle with strong evidence of a unilateral infection of one kidney and ureter—i.e., a clear and normal efflux from one side with a purulent efflux and an infected orifice on the other side—nephrectomy and ureterectomy followed by the use of T.R. are indicated.

Method of employment.—The T.R. is given hypodermically with a sterilised syringe. Wherever possible I keep the patient in bed or, at all events, in the house for the initial stages of the treatment, the temperature and general symptoms being carefully noted. I now commence with a dose of $\frac{1}{10}$ th milligramme, and give increasing doses every other day until a definite reaction is obtained, usually marked by a rise of temperature of two degrees or so, some malaise, and a slight increase of pain and frequency of micturition. The dose is then reduced to that quantity which apparently causes no reaction and is given steadily once a week for long periods; should a definite reaction again occur the dose is once more diminished and given at longer intervals. My experience of T.R. in the treatment of tuberculosis is limited to the urinary system, and here I consider the clinical evidence is a sufficiently delicate indication. Over-dosing causes such definite symptoms of loss of ground, evidenced by increased pain, hæmaturia, and frequency of micturition, with a heightened temperature and loss of body weight, that they cannot be overlooked; they correspond with Wright's negative phase of the opsonic curve, and I feel content that, by a careful watch upon these symptoms, the dosage can be sufficiently accurately regulated. During the progress of treatment the patient's weight and temperature should be carefully noted, together with the subsidence or progress of the symptoms particularly applicable to the organs affected, and it is perhaps hardly necessary to add that all hygienic and dietetic treatment found beneficial in tuberculosis generally should be followed. In those cases which show favourable progress the number of tubercle bacilli found in the urine steadily decreases. A cystoscopic examination from time to time conducted with the precautions to which I have alluded will show the extent of healing which has taken place.

RESULTS.

I have included in this paper no cases which have not been under observation for more than one year, but even so I feel that it is impossible to speak with any certainty as to the results obtained in those few cases which have apparently regained perfect health. Tuberculosis of the urinary system has such long periods of latency that he would be bold indeed who prophesied a permanent cure in patients apparently well for a year or more. This is evidenced by a case of this series in which the patient has suffered from tuberculosis of the bladder for at least 17 years, during which time he has had periods of a year and more with almost entire absence of symptoms; but the renewed interest taken in tuberculin renders any record of results, whether good or bad, of sufficient importance to warrant their publication.

[Mr. Pardoe appended to his paper a tabular statement giving full details of all the cases. The statement was too long for reproduction in our columns, but the subsequent paragraphs summarise its contents:—]

In all 21 cases I have been able to obtain information up to within a few weeks, with one exception. I have not included a considerable number of patients who have disappeared during the course of their treatment and whose movements I have been unable to trace, although many of them were in a very encouraging condition when lost sight of.

Of these 21 cases five appear to be cured. Bearing in mind, however, the great tendency to relapse shown by tuberculosis of the urinary system I prefer to call them only apparent cures. Four cases show a very marked improvement, evidenced by absence of pain, diminution of the frequency of micturition, absence of hæmaturia, and cystoscopic evidence of the amount of such improvement. Six cases show no improvement. In some of these I consider that T.R. has not had a fair trial, particularly in Case No. 14. This woman was subject to outbreaks of drinking, lasting sometimes for two or three weeks, during which she would consume from one to three bottles of whisky a day. The injections had to be stopped during these drinking bouts and for some time after. In one or two other cases also the injections were not continued regularly, owing to the patients feeling so much

better that they stopped away, only returning when their symptoms began to reappear. Six cases died. In one of these I have no doubt T.R. was the direct cause of death. T.R. should not have been given in this case at all and it was only at the patient's urgent request that I gave him five injections. He had a very severe reaction with $\frac{1}{10}$ th milligramme, and as I was certain that both ureters were infected I refused to give more. He insisted on having further injections on returning home to the country and died very rapidly with complete suppression of urine. In all the fatal cases the infection was somewhat extensive. I append here in tabulated form the results I have obtained up to date:—

Died. Case	No improvement. Case	Much improved. Case	Apparently cured. Case
No. 1	No. 9	No. 3	No. 2
7	13	6	4
11	14	8	5
15	16	12	10
20	17	—	18
21	19	—	—

CONCLUSIONS.

My experience with other methods of treatment has been disappointing in the extreme, for I cannot call to mind any case of apparent cure of vesical tuberculosis by operative measures and the published records of such cases are indeed few. I therefore think that, so far as these series of cases go, it is not unduly optimistic to claim that the results gained by injections of T.R. are at least as good as those by any other method. It will be noted that the earlier the case is brought under treatment, or, to put it in another way, the more circumscribed is the infection, the better are the results. In not one case where the cystoscope showed diffuse infection has very much benefit been noted. The cases of apparent cure occurred where only a small amount of bladder surface appeared to be involved. I do not think that in T.R. we have a perfect remedy for tuberculosis of the urinary system but for vesical tuberculosis it seems to me the best remedy at our disposal. Before I used it I felt little or no hope of effecting much improvement but I now feel that in some cases there is hope of a cure and in a larger proportion of cases of, at all events, great improvement. I shall venture to ask permission of the Fellows of this society to bring before them the later histories of these cases, together with those of patients whose treatment has been too recently commenced to be mentioned to-day, unless the onward march of science in the meantime brings to us most happily a more perfect and hopeful method.

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ÆSCULIN IN CONJUNCTION WITH FINSEN LIGHT IN THE TREAT- MENT OF LUPUS VULGARIS.¹

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EXPERIMENTS in sensitising animal tissues to the action of light have been carried out by Georges Dreyer in Copenhagen, who read a paper on the subject before the Royal Danish Academy, and also by W. J. Morton of New York. Dreyer used a 30-ampère arc lamp concentrating the light through a train of quartz lenses similar to those in use in Finsen's apparatus and as the sensitising agent a 1 in 4000 solution of erythrosin. Very considerable differences were shown in sensitiveness between sensitised and non-sensitised cultures and I would refer to his paper for the interesting table of his results. Among other points he has shown that cultures of bacillus prodigiosus sensitised with erythrosin are sterilised in the yellow green rays of a spectrum cast by a quartz prism. Morton states that he has used quinine bisulphate and æsculin excited by radium and by x rays; of the two he preferred excitation by radium. I was at first deterred from using erythrosin by the fear that a permanent stain might remain after its injection and later

¹ A paper read at the meeting of the British Electro-Therapeutic Society held at Leicester on July 27th, 1905.

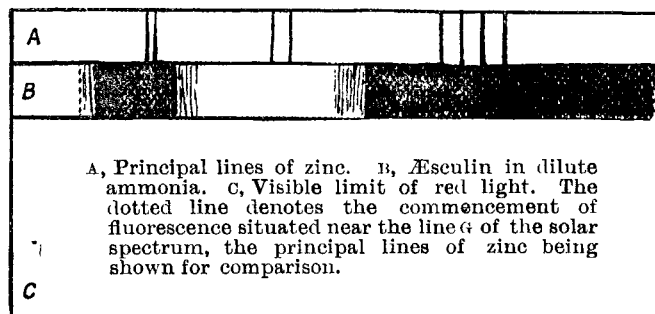
by the information given me by Dr. Reyn of Copenhagen that when injected in a strength of 1 in 4000 severe reactions followed its use with Finsen light, causing much pain and often sloughing of the tissues.

Some here present may recollect a slide shown by Dr. H. E. Gamlen when he read a paper before this society last November of a patient who, following an injection of erythrosin in the neck and an application of Finsen light, had a deep ulcer develop which had resisted all methods of healing during several months and even then remained unhealed. I shall again refer to this action of erythrosin in discussing that of æsculin. I have used æsculin excited to fluorescence by a 20-ampère arc light passing through the Finsen-Reyn apparatus. Æsculin ($C_{15}H_{16}O_9$), discovered by Minor in 1830, is a glucoside obtained from the inner bark of *Æsculus hippocastanum* (horse-chestnut), especially in March, before the buds open. It is bitter, very sparingly soluble in cold water but easily in boiling water, coagulating quickly again on cooling. If the solution is made slightly alkaline by the addition of 2 or 3 per cent. of sodium carbonate the coagulation is prevented. In two or three days after a solution is made it turns dark in colour and it should therefore be used freshly made. Heat at $230^{\circ}C$. resolves it into glucosan and æsculitin. Sonnenschein gives as a delicate test for it that if it is agitated with a small quantity of nitric acid it yields a yellow solution which assumes a deep blood red colour on addition of ammonia.

Æsculin is one of the highest fluorescent bodies in existence to our knowledge and I believe passes through the system unchanged. Calvi attributed convulsive effects to it in doses of two milligrammes, but Amore afterwards considered this due to the glycerine used to dissolve it. Morton has given it in one-grain doses without ill-effects. I gave myself a hypodermic injection of five minims of a 5 per cent. solution rendered alkaline by the addition of 3 per cent. of sodium carbonate. No pain was caused nor did any constitutional disturbance follow. Fifteen minutes after the injection the urine showed slight evidence of fluorescence. Another specimen passed an hour after the injection was very distinctly fluorescent and this increased markedly during four days that I kept it, leaving a fluorescent deposit on the side of the test-tube. It was evident that as alkaline changes took place in the urine it became more fluorescent.

Doubt was expressed by a member of this society at a recent meeting as to whether fluorescein and like bodies did actually fluoresce in animal tissues and with this object I had injected under the shaved skin of a guinea-pig five minims of a 5 per cent. solution of æsculin. Having removed nearly three square inches of skin together with the subcutaneous tissue and some muscle and stretched it over a ring I passed the 20-ampère carbon arc light through the Finsen Reyn apparatus on to it exactly as if a patient was being treated and found the whole of the skin (one millimetre thick) and subcutaneous tissue very fluorescent. Where the muscle remained attached the fluorescence was not so evident, the tissues there being at least three millimetres thick.

With regard to the absorption spectrum of æsculin, G. G. Stokes in vol. clii. of the Philosophical Transactions, 1862, gives a diagram showing a band between G and *h* *h* of the solar spectrum.



C. G. Schmidt² gives a band from wave lengths 410 to 257, the maximum of intensity being at wave length 361; from wave length 257 the absorption increases in intensity in the extreme ultra violet. Nicholls and Merritt³ give the position of the absorption band as from wave length 480 to 340 but state that they put twigs of horse-chestnuts into water and did not attempt to isolate the glucoside itself.

Being such a fluorescent body only a small dose is necessary, and in practice I have used from one to five minims of a 5 per cent. solution hypodermically. The solution is better used within two days of being made. The needle is passed only just through the skin—not deeply into the tissues—and the injection is made immediately under the spot to be treated. The reaction following an ordinary Finsen sitting is usually over by the third day, but after sensitising with æsculin I have observed it to last from four to seven days longer. It has also seemed to me that æsculin remains in the tissues for some days, as I have noticed that Finsen sittings have had stronger reactions than normal when given in the neighbourhood of an injection even from four to five days afterward.

In lupus vulgaris cases I have now given considerably over 100 injections, no ill effects following in any instance; and I think the chief value of æsculin in this disease will be found in the treatment of obstinate isolated tuberculous nodules that sometimes remain after a preliminary course of ordinary Finsen treatment has cleared up the disease in the surrounding structures. Such nodules I have seen rapidly disappear after being sensitised, though several previous applications of the light had been made. I have also found æsculin given in this way to be of material assistance in softening thickened fibrous scars in character similar to keloid that so frequently follow the scraping of lupus patches and which form such excellent harbouring ground for tuberculous nodules from which they are very difficult to eradicate.

Now, how can the action of æsculin be explained? It seems to me to be a purely physical one. The term fluorescence proposed by Stokes is applied to the conversion of the invisible ultra-violet rays into visible ones; that is, their refrangibility is lowered, their wave length being increased. Certain substances, both fluid and solid, emit a glowing light in virtue of their absorption of ultra-violet rays, among the most powerful of these, as stated above, being æsculin. In the original Finsen or Finsen-Reyn apparatus a concentrated light combining various rays is used, the principal rays having a therapeutic value being the blue, violet, and ultra-violet. But it is known that the ultra-violet rays, though having the strongest therapeutic and bactericidal action, have very slight power of penetration into animal tissues; consequently the remarkable results that have been admittedly achieved in the treatment of lupus by Finsen's method are probably due chiefly to the blue and violet rays. Now I would suggest that æsculin, a powerful absorbent of ultra-violet rays, gives them off again in the wave lengths corresponding to the violet and blue, and by causing a great local excess of concentration of these rays at the time the light is applied and by its prolonged fluorescence in the tissues afterwards clears up the tuberculous nodules more rapidly than the arc light alone. Whether this clearing takes place by the direct bactericidal action of the rays or by phagocytosis is a question which I shall not enter into here, but probably each has its sphere and the ultimate result may be due to a combination of the two.

The effect of this concentration and prolonged action is shown by the yellow-green rays in Dreyer's experiment with erythrosin, but an interesting point arises in connexion with the practical use of this substance and one that I should like to hear explained—viz., the destruction of tissue that I have mentioned frequently takes place when erythrosin is made to fluoresce in it. The longer wave lengths of the yellow-green portion of the spectrum are supposed to have little therapeutic effect, whereas those of the short blue-violet are acknowledged to have a strong action, yet æsculin, which gives off the latter, I have shown to be free from ill-effects, while erythrosin giving off the yellow-green proves painful and destructive.

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HUSBAND'S LIABILITY FOR WIFE'S MEDICAL TREATMENT.—In the City of London court on Dec. 7th, Mr. G. J. Cooper of Bermondsey sued the husband of a late patient for £2 7s. 6d., being the fees due after attending the wife on 19 occasions. The defendant pleaded that he did not employ Mr. Cooper, who was called in by the patient's mother at the latter's house from which she was removed at last to a lunatic asylum. Judge Rentoul, K.C., told the husband that the law was that if a wife was staying away from home and she was taken ill any medical man called in by her host could compel the husband to pay the bill; therefore he gave judgment for the plaintiff with costs.

² Annalen der Physik und Chemie, No. 5, 1896.

³ The Physical Review, New York, vol. xix., 1904.