worthy, both on account of its severity and the splendid result obtained.

During the past three and a half years I have had under my care in this hospital many cases in adults. The local treatment adopted varied from time to time. A group of cases was treated by gonococcal vaccine in addition to local measures, but whether vaccine were given or not, there seemed to be little difference in the results taken as a whole. Gradually, however, I became convinced of the uselessness of silver nitrate in combating the disease, and discarded it in the more severe types with much swelling, for in these it invariably appeared to aggravate the condition.

In gonorrhoeal ophthalmia the most dangerous period is during the first few days of the infection, when, owing to the swelling of the eyelids and bulging chemotic ocular conjunctiva, the cornea is obscured over the whole or most of its area, and the removal of discharge from its surface is made difficult or impossible. The continued bathing of the cornea in this discharge introduces the most serious factor, for the corneal epithelium is damaged principally by the action of the gonococcus or its toxins, while the nutrition of the cornea as a whole is also injuriously affected to some extent by the excessive swelling.

It seems certain that the main effort of treatment in this stage should be directed towards controlling and abating the violent reaction to the gonorrhoeal infection, by bringing about a rapid decrease in the conjunctival swelling, and so allowing of thorough yet gentle cleansing of the whole eye by non-irritating collyria. The use of any drug which by its action would tend to increase the swelling is contra-indicated.

Colloidal manganese appears to act in the manner required. It was recommended and given by Captain J. E. R. McDonagh in my last three cases with favourable results. The first case was not of great severity, but the action of the drug appeared satisfactory. In the second case it was not given till corneal ulceration had set in, but the eye healed rapidly, and swelling and discharge abated during its use. The third case was of a most virulent type, and the effect of colloidal manganese, given for the first time from the beginning, was most striking.

Pte. J., aged 24, admitted December 24th, 1918, with gonorrhoeal ophthalmia of the left eye. Two days previously he felt his eye pricking, and the following morning—the day before admission—the eyelids were swollen and difficult to open. On admission both lids were greatly swollen and almost solid, so that they could only with difficulty be separated. There was great tenderness and pain, and the surrounding cheek was also red and swollen. On opening the lids the cornea was found to be completely hidden by overlapping folds of oedematous bulbar conjunctiva. There was an abundant discharge of thin pus. The eye was bathed with warm boric lotion every hour by day, and every two hours by night, and 10 per cent. argyrol was used every six hours. An injection of 1 c.cm. colloidal manganese was immediately given by Captain McDonagh intramuscularly into the buttock. On December 25th there was a slight improvement, and a little part of the cornea could be seen. The lids were more easily parted. On December 26th he still had slight pain; on December 27th he was given colloidal manganese 1 c.cm. as before, and by the following morning he expressed his delight in the almost complete absence of pain. The change was striking: all swelling of the bulbar conjunctiva had completely vanished; the oedema of the eyelids had greatly lessened, and the discharge also had become noticeably less in volume. The cornea was perfectly clear, with its epithelium intact over the entire surface, and the eye was apparently out of danger. On December 31st a third and last injection of colloidal manganese 1 c.cm. was given, and by January 9th the conjunctiva had become almost normal, and discharge had practically ceased, except for gunning of the eyelids after sleep.

The appearance presented by this case on the day following the second injection of colloidal manganese was in truth surprising. In a fairly wide and long experience in the treatment of gonorrhoeal blenorrhoea it had never previously been my good fortune to witness such a dramatic change. No local measures with which I am acquainted would have brought about such a satisfactory termination.

It is hardly necessary to emphasize the danger of drawing inferences from results obtained from any remedy in a small number of cases. Prolonged use of the drug is necessary before definite conclusions which will stand the test of time can be reached. Nevertheless it is well to avoid cultivating the habit of mind which sees the perfection of achievement in everyday methods already in use, and refuses to recognize their defects. Where treatment is too often followed by indifferent results, as in

gonorrhoeal ophthalmia, the need for fresh endeavour becomes insistent. In future we shall use colloidal manganese in the hope that it represents a decided advance over former methods of treatment; in any event we seem to have acquired a valuable therapeutic ally and one worthy of extensive trial.

I have to express my indebtedness to Captain McDonagh for his valuable assistance in the treatment of these cases; and to Lieut.-Colonel W. Turner, C.M.G., O.C. Connaught Hospital, for permission to publish these notes.

METHYLENE BLUE IN PURULENT DISCHARGE FROM THE EYE SOCKET.

BY

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INJURIES to the eye have been of very frequent occurrence in the war, and enucleation has had to be performed in a large number of cases. After an artificial eye has been supplied, the soldier has in many instances suffered from purulent discharge of the conjunctiva in the socket, particularly if the artificial eye has been worn for a long time, or has become rough and irritating for any reason. These sockets have proved themselves very difficult to treat; the ordinary methods of treatment, such as zinc sulphate, alum, or the silver preparations have been found most unsatisfactory.

Adams,¹ in his monograph on the use of methylene blue in eye work, shows that the drug is of value in cases of conjunctival discharge due to the *Staphylococcus aureus*, the more usual lines of treatment having failed.

In the ophthalmic department of this hospital methylene blue (1 in 1,000 saline solution) has been employed as the regular routine method of treatment in cases of discharging eye socket, and the results obtained have been so striking and satisfactory that we were led to inquire how the drug exercised its effect—whether there was a definite germicidal action, and if so, whether there was a selective action for one micro-organism more than another. The present investigation was undertaken at the suggestion of Major Maitland Ramsay, the clinical results having been observed by him in these wards over a lengthened period.

For the bacteriological investigation, carried out in the pathological department of the hospital, nine cases of purulent discharge from the eye socket were taken. They were not selected—save that they were illustrative cases in which actual discharge was present. Some had been under treatment with methylene blue for a time, but in none had the discharge completely stopped. Treatment was suspended in every case for twenty-four hours or so in order that the discharge might be as abundant as possible without prejudicing the welfare of the patient. A feature of the treatment by methylene blue is that although the discharge vanishes after the drug has been in use for a comparatively short time, it is necessary to continue the treatment for a further period (say a fortnight) after the discharge ceases to be obvious to the naked eye, in order to prevent recrudescence.

In each case to be investigated direct microscopic films were made, and agar slopes inoculated; the first step in the research was to find the prevailing organism in the conjunctival discharge. Agar medium was employed for culture throughout, and the results must necessarily be expressed on limited lines. The possibility of demonstrating the presence of micro-organisms which flourish on different media is allowed for, but the finer points of research into the germicidal valency of chemical substances belongs to the expert bacteriologist.

The direct films made from the socket on microscopic examination were practically all negative, as is often the case in films of conjunctival discharge. The agar slopes were incubated for twenty-four hours. Well-marked growth was found in the case of two cultures only, and these were selected for further experiment. In all cases in which any growth appeared the prevailing organism was found to be *Staphylococcus aureus*.

In each of the two cultures selected for further investigation a subculture on agar was made in order to procure

an active growth in the pure form. As the subsequent procedure was the same for both, details will be given for one experiment alone.

Experiment.

1. The subculture of *Staphylococcus aureus* was taken at the end of twenty-four hours' incubation, a good growth being present.

2. A bacterial emulsion was made by rubbing down the organisms (adhering to the end of a platinum loop which had been introduced into one of the larger colonies) in 1.5 c.cm. sterile saline solution contained in a sterile test tube. The turbidity of this emulsion was barely visible to the naked eye, and it was calculated that the micro-organisms were present in considerable dilution.

3. Three sterile test tubes were taken, and into each was placed 0.5 c.cm. methylene blue, obtained from the stock solution in daily use in the wards.

4. To each tube containing the drug 0.03 c.cm. of the bacterial emulsion was added, the resultant mixture being well shaken to bring the organisms into intimate association with the methylene blue.

5. At the end of half an hour, six hours, and twenty-four hours respectively, these solutions (which had been shaken frequently) were taken, and agar slopes inoculated by making successive strokes with a platinum loop which had been introduced into the emulsion-methylene blue mixture.

6. The agar slopes were examined at the end of twenty-four hours, and forty-eight hours.

Results.—The half-hour and six-hour exposures on agar yielded practically the same result, namely, a diffuse growth of *Staphylococcus aureus* at the end of twenty-four hours' incubation. The twenty-four hour exposure showed no growth visible to the naked eye at the end of twenty-four hours' incubation. At the end of forty-eight hours' incubation, however, a few well developed colonies of *Staphylococcus aureus* were easily seen by the naked eye.

The experiments were repeated several times, and gave the same results.

Summary.

1. The prevailing micro-organism obtained by agar culture from nine cases of purulent discharge of the eye socket was found to be *Staphylococcus aureus*.

2. Methylene blue, although proved to be very active clinically in cases of discharging eye socket, was found to have comparatively little bactericidal action upon *Staphylococcus aureus* obtained from the discharge—0.03 c.cm. of a very dilute emulsion of the micro-organism, after even twenty-four hours' exposure to the drug, still giving a number of colonies of growth after incubation.

REFERENCE.

¹ P. H. Adams, D.O.: On the Use of Methylene Blue in Eye Work, *The Ophthalmoscope*, vol. xiv, No. 2, February, 1916, p. 78.

PRELIMINARY NOTE ON THE RESPONSE TO CALCIUM SHOWN IN MANIACAL STATES.

BY

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ACTING on deductions drawn from physiological observations I resolved to test the effect of the exhibition of calcium in persons suffering from various degrees of excitement. For this purpose I chose the lactate as the most suitable salt in order to have the action of the calcium ion unimpaired by other elements. Moreover, as the lactate is easily soluble in hot water and remains in solution when cold, a convenient means of administering the drug is available.

I do not propose in this communication to discuss the mode of action of the element in these cases; this and other cognate matters will be dealt with fully in another communication. I wish to report merely the effects observed not only in the mental state but also in the circulatory system.

The action of the drug became evident at least during the twenty-four hours following its exhibition. The acute mental symptoms were alleviated without the production of the stupor so commonly observed resultant from the action of the "sedative" drugs—if, indeed, they produce any effect at all in many cases. The circulatory response has been equally interesting. Instead of the rapid, at times almost uncountable, pulse with its flaccid artery and variable but always low systolic pressure, the pulse becomes

slower, the artery normally constricted and the pulse wave stronger, indicative of an improved action of the ventricular myocardium.

The action of the drug has been equally satisfactory in the distressing restlessness and excitement of agitated melancholia and confusional states as with the simple mania. Those cases in which influenza has been assigned as the principal cause have reacted well to the drug. These cases had resisted ordinary sedative treatment, but with this definite addition of calcium to the diet—for that is what the treatment amounts to—a vicious circle seems to have been completely broken, and they are making good progress towards recovery.

Many of the other cases in whom, owing to the duration of the character of the mental disorder, complete recovery can hardly be expected, have nevertheless shown amelioration of the more acute symptoms, which may well be a determining factor in leading to an improvement of variable degree.

So far I have contented myself with giving 10 grains three times a day with food, and when a response has been obtained dropping the dosage to 5 grains. In one particularly distressing case of agitated melancholia in addition to the doses by day one or two doses have been given at night. It was interesting to note that in one case of mania with diarrhoea not only was the restlessness and excitement allayed, but the number of stools passed fell from six to one.

So far no untoward effects of any kind have been observed, and, considering the small doses employed, these can hardly be expected if careful observations on the pulse are made.

The Lumleian Lectures

ON

CEREBRO-SPINAL FEVER.

DELIVERED BEFORE THE ROYAL COLLEGE OF
PHYSICIANS OF LONDON.

BY

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LECTURE I.

(Abstract.)

In his first lecture Sir Humphry Rolleston dealt with the history and etiology of cerebro-spinal fever. Examining the history from 1805 he distinguished five periods, the fifth beginning in 1903. New York suffered severely in 1904-5, Silesia in 1905-7, and France in 1909-10. In Great Britain outbreaks occurred in 1907 in Belfast, Glasgow, and Edinburgh. Compulsory notification was permanently established in 1912, and the cases and deaths subsequently were as follows:

Civil Population.

Years.	Cases.	Deaths.	Case Mortality (per Cent.)
1912	272	142	52.2
1913	304	163	53.6
1914	300	206	68.6
1915	2,343	1,521	64.9
1916	1,278	833	65.6
1917	1,385	906	65.4

There was therefore no question that the disease increased in this country after the outbreak of war. The belief that there had been a change of type of the disease was supported by Dopter's observation that in France the type of infecting organism underwent a change during the war. Netter correlated the greater frequency of septicaemic cases and lesions such as rashes, arthritis, iridocyclitis, with this alteration of the infection from Type A (Gordon's Types I and III) to Type B (Gordon's II and IV). The observations of Kennedy and Worster-Drought suggested that Types I and III (Nicolle Type A) were more virulent as regards the meninges and Types II and IV (Nicolle Type B) specially prone to cause septicaemia and