

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

extra-meningeal metastases. But in a recent small outbreak of 10 cases due to Type II under the lecturer's own observation, the meningitic manifestations were very severe. Adshead analysed 49 cases in which Gordon's types of meningococci had been determined, but did not feel justified in drawing any definite conclusions.

The periods between epidemics were bridged over by sporadic cases; at or before the commencement of epidemic outbreaks these sporadic cases became more frequent. The special advisory committee upon bacteriological studies of cerebro spinal fever during the epidemic of 1915, adopting Dopter and Arkwright's view, concluded that the epidemic was not one of cerebro-spinal fever as such, but what might be termed a "saprophytic epidemic" of the meningococcus in the throats of the population, cerebro-spinal fever being an epiphenomenon of this epidemic, due to a secondary systemic invasion from its saprophytic focus in the nasopharynx, occurring in spare and isolated instances which, as a rule, appear to be unconnected with each other.

Epidemiology.

As the vast majority of the cases in Great Britain occurred during the first six months of the year it might be suspected that meteorological conditions exerted a definite influence on the incidence of the disease. Sudden alterations in the atmospheric temperature had been emphasized by Sophian and Dopter as responsible for the outbreak of cases, and the lecturer had received the same impression at the Royal Naval Hospital, Haslar, in 1914-17, but investigation of the 93 cases occurring at large naval dépôts during the first three months of 1915 did not justify any positive conclusion.

Compton's views on the meteorological conditions were quoted fully, the conditions favouring pneumonia outbreaks, as described by Herringham, mentioned, and a comparison of the curves of pneumonia and of cerebro-spinal fever made. Unless it could be convincingly proved that the outbreaks of cerebro-spinal fever were closely and accurately correlated with changes in the meteorological conditions—and that it was not so appeared clear from consideration of various views—it became more probable that the conditions prevalent during the months of greatest incidence acted by increasing the carrier rate or the power of carriers to spread infection—namely, by coughing—or by both means, and so exposing a larger number of possibly susceptible persons to the opportunity of systemic infection. The conditions favouring a high carrier rate were (a) prevalence of colds and coughs, which enabled existing carriers to infect others; (b) close contact of individuals such as occurred in cold weather. The observations of Dr. J. A. Glover (published in the JOURNAL of November 9th, 1918, p. 509) showing the influence of overcrowding in increasing the carrier rate were quoted. In discussing the question of the relation of the disease to campaigns it was pointed out that there was little information as to increased prevalence of the disease during previous wars. In the French troops in this war the disease became less frequent—the rate in 1915 being 4.3 per 10,000; in 1916 it was 1.8 per 10,000, and in 1917 1.5 per 10,000. For the army in this country the figures were as follows:

Army at Home.

Year.	Cases.	Deaths.	Case Mortality (per Cent.)
1914*	50	31	60
1915	1,195	586	49
1916	967	430	44.6
1917	1,337	593	44.3

* From September 19th to December 31st, 1914.

In the British Expeditionary Force in France the disease began to appear widely in a scattered fashion in January, 1915, at the same time as in troops in this country. The outbreak in 1915, when the available serums were useless, was the worst in France; the mortality was then about 50 per cent., and during the war probably never fell below 35 per cent. The disease first became prominent among the military population in this country, and the civil population then followed suit; the increase in the incidence of the civil cases during the

war was striking; in 1915 the number of civil cases was eight times that of 1914, and in 1916 and 1917 four times that of 1914 (Reece). Evidence with regard to the relation of colds and catarrhal affections to cerebro-spinal fever was conflicting. The special Advisory Committee of the Medical Research Committee on the bacteriological studies of the epidemic in 1915 considered that the relation with catarrhs and the disease was fortuitous, as both had a similar seasonal prevalence, the relation being the same as that between catarrh and the prices of coal. On the other hand, the view that catarrhal throat affections, by inducing coughing and sneezing, spread meningococcal infection and so increased the carrier rate and the chances of systemic infection, as urged by Pringle, seemed highly probable. The prevalence of colds in the population would thus favour the outbreak of cerebro-spinal fever, but it was not necessary that cerebro-spinal fever patients should have had colds or naso-pharyngitis.

The evidence as to the depressing effect of recent acute affections, such as influenza, mumps, and measles, in disposing persons to meningococcal infections was also conflicting. The most susceptible age was from birth to 5 years, and in some epidemics 80 to 90 per cent. of the patients had been under 15 years of age; in the Dantzic epidemic of 1865, for example, 93 per cent. were under this age. It was generally estimated that half the total cases occurred in the first five years of life; in England and Wales, during 1914, 51.4 per cent. of the cases were in children under the age of 5 years, and 72.4 per cent. under 10. But in 1915 and 1916 these percentages (30 and 48.8, and 38.7 and 54.8 respectively) were much lower, although the military cases are not included (Reece). Compton, who connected the greater fragility and delicacy of the nasopharyngeal mucosa in children with their susceptibility to infection, stated that the least susceptible age is between 35 and 40 years. Statistics favoured the opinion that the disease occurred more often in males, especially in young males.

Mode of Spread of Infection.

The actual spread of infection was mainly due to droplets expelled from the nasopharynx in coughing, sneezing, and violent expiratory efforts, so that the carrier's power for harm depended on the existence of cough, etc., on the number of meningococci, and also largely on their being of an epidemic type. Infection might also be conveyed directly from mouth to mouth, as in kissing. The question of the importance of prostitutes as meningococcal carriers required investigation. Other methods of spread of infection were less important or very doubtful. Adami had recently spoken of the spread of infection through drinking vessels, partially or imperfectly rinsed, in crowded canteens and refreshment booths.

When a carrier lived in close contact with healthy individuals the carrier state was prone, especially under conditions of overcrowding, to be conveyed to others, and these new carriers acted in like manner. Among the individuals thus exposed some might, from diminished resistance, become systemically infected, and, as Glover had shown, this should be expected when the carrier rate, normally under 5 per cent., rises to the danger line of 20 per cent.

Path of Meningeal Invasion.

Three paths by which the meningococci reached the meninges were discussed: 1. Direct invasion through the nasopharynx and accessory sinuses through (a) the sphenoidal sinuses; (b) the cribriform plate of the ethmoid; and (c) through the Eustachian tube to the middle ear and so to the brain. 2. Lymphogenous infection along the spinal nerve roots in the cervical, thoracic, and abdominal regions. 3. Infection from the blood stream. The conclusion drawn was that while the hæmic infection of the meninges appeared to be applicable to the majority of the cases, the possibility that in certain instances infection might pass by other routes, such as through the cribriform plate of the ethmoid or the sphenoid, could not be entirely excluded. In connexion with the path of infection of the meninges the question arose where the meningitis began—whether it started in the choroid plexuses of the lateral ventricles (as seemed to be the general view), in the spinal meninges, or in both situations simultaneously.

Meningococcic Septicaemia.

Sir Humphry Rolleston concluded his lecture by discussing meningococcic septicaemia, which, he said, might present several variations from the short initial invasion of the blood by meningococci, which probably preceded infection of the meninges in most, if not all, of the cases of meningococcic meningitis. He continued as follows:

Possibly cases of true meningococcic septicaemia are only more commonly recognized now than formerly, but Netter has suggested that Dopter's observation that whereas before the war 96 per cent. of the cases of meningococcic meningitis were infected with the meningococcic Type A (Gordon's I and III types), a change has taken place, so that now the parameningococcus, or Type B (Gordon's II and III), is responsible for an equal, if not a larger, number of the cases, may be correlated with an increased incidence of meningococcaemia and meningococcic manifestations in the skin, joints, and eyes. Brulé also considers that parameningococcaemia (due to Type B) is more frequent and more severe than meningococcaemia (due to Type A).

Meningococcaemia appears to have been first established by Gwyn in 1899 in a case of meningitis with arthritis. Salomon in 1902 detected meningococci in the blood eight weeks before meningitis supervened; in the following year Warfield and Walker described the first case of meningococcic endocarditis with septicaemia; a fulminating case of meningococcaemia also without meningitis was recorded by Andrewes in 1906, and in reviewing the cases two years later Duval summed up in favour of the septicaemia being secondary to the meningitis, the reverse of the present opinion. Lüdke described a case of meningococcic septicaemia in which in addition streptococci were obtained by blood culture.

Portret distinguished four kinds of meningococcaemia: (i) Without meningitis, (ii) preceding meningitis, (iii) with metastases, (iv) without metastases. The following forms of meningococcic septicaemia may be described:

1. In a certain number of cases a fulminating meningococcaemia proves fatal before meningitis has had time to occur, and lumbar puncture, if performed, gives exit to clear fluid without any meningococci or increased cell content. At the necropsy meningococci can perhaps be obtained from the fluid in the ventricles of the brain, but there is no exudation. The clinical features of these cases are severe toxæmia, often at the onset, with a low temperature, followed by fever and perhaps hyperpyrexia, rapid pulse and respirations, and extensive haemorrhages into the skin, mucous and serous membranes, and adrenals. The clinical picture may suggest the "acute abdomen," such as internal strangulation, intussusception (Pybus), or Henoch's fulminating purpura, haemorrhagic fevers.

2. Abortive cases in which a blood infection is overcome after a short time by natural immunity, though commonly assumed to be frequent, are difficult to prove. Cases of febrile meningococcic purpura without meningeal symptoms, or presenting meningeal irritation which, as shown by lumbar puncture, is not due to meningitis, and may therefore be explained as meningism, come under this heading. Sainton and Maille's case with a measly eruption, synovitis of two joints containing meningococci, and a positive blood culture but no meningitic symptoms, the whole illness lasting about a week, belongs to this group of abortive cases. In order to determine the incidence of these abortive cases during an epidemic Maxcy selected 27 cases with fever, headache, and malaise, but without petechiae, and made blood cultures which were uniformly negative. Doubt is thus thrown on the assumption of their frequency, but further investigations of this character are desirable.

3. Intermittent meningococcic fever due to septicaemia may (a) last for weeks without any meningitic symptoms ever developing. In Liebermeister's case the disease lasted four months and in Bray's case, complicated by chronic pulmonary tuberculosis, there was fever for five months and recognized meningococcaemia for three months. Though striking, they have not been very often recognized. Netter had five examples among his 368 cases, and Brette collected 22 cases in 1918. The attacks of fever may be quotidian or tertian and in the intervals the patient may feel well. The disease may resemble malaria, quotidian or tertian, or enteric fever—Netter's pseudo-malarial and pseudo-typhoid forms. The attacks of fever may begin with a rigor and

end with sweating, be accompanied by splenic enlargement; joint pains and orchitis may occur, and rashes, such as polymorphic erythema or erythema nodosum, herpes or papules, especially on the lower extremities or around the joints, or petechiae may be present. But the disease may run its course without any cutaneous manifestations (Zeissler and Reidel, Worster-Drought and Kennedy). In exceptional instances malignant endocarditis is due to infection with the meningococcus (Warfield and Walker, Cecil and Soper, Worster-Drought and Kennedy).

(b) In another group septicaemia follows the subsidence of meningococcic meningitis. Brulé records a case with septicaemia of two months' duration with purpura and positive blood cultures on five occasions. Lancelin's patient had meningococcic meningitis, and after an afebrile period of four days had fever imitating malaria for seven days and then yielded to serum; meningococci were not obtained from the blood, but the presence of purpura rendered septicaemia highly probable. Among 126 cases Landry and Hamley detected two cases of post-meningitic septicaemia.

(c) During the course of intermittent meningococcic fever there may be transient meningitic symptoms; thus, Maxcy describes a case with transient rigidity of the neck, which appeared a week after the onset and rapidly passed off.

(d) In an allied group of cases the septicaemia is prolonged, but is eventually followed by meningeal infection; in Ainé and Chéné's case the pseudo-malarial stage with splenic enlargement lasted for four weeks before the onset of meningitis; and in Serr and Brette's two cases lumbar puncture was first performed after four and two months' fever, and cures rapidly followed the intravenous injection of serum.

A correct diagnosis is seldom made in the absence of meningitic symptoms. Blood cultures should be taken during the febrile paroxysm.

The Milroy Lectures

ON

**HALF A CENTURY OF SMALL-POX
AND VACCINATION.**

DELIVERED BEFORE THE ROYAL COLLEGE OF
PHYSICIANS OF LONDON.

BY

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**CONTROL OF SMALL-POX IN THE PRESENT
DAY (continued).****VII. LOCAL CO-OPERATION AND CENTRAL CO-ORDINATION.**

A duty that should not be neglected is to notify local authorities in the neighbourhood, especially if any contacts are supposed to have travelled into their area. The date of exposure to infection of such contacts should always be stated to the medical officer so as to guide his action. If in any case there has been an exodus of navvies from constructional works or of vagrants from a lodging-house, the police of surrounding areas, as well as the medical officers of health, should be informed and a search instituted for contacts. Often the name of the navy in such circumstances is of no avail. Some of them for various reasons seem to use a new name for every new job.

Dr. Boobyer of Nottingham adopted a very systematic scheme of notification to various parties within his own area who might utilize information sent to them. The name and address of every fresh patient was furnished daily to general and special hospitals, to the post-office surgeon, the Charity Organization Society, the guardians, the Education Committee, the city librarian, the health visitor, the owners or rent collectors of infected houses, the vaccination officer and public vaccinator, and various municipal officers.

Under orders by the Local Government Boards of England and Scotland every small-pox case individually is to be reported as it occurs. The army, navy, and air force authorities are notified at once if concerned, an inspector is usually sent, and necessary inquiries are carried back to other districts or other countries. Small-pox abroad is followed to the extent that information