THE ANTIBODY CONTENT OF THE CEREBRO- SPINAL FLUID IN MENINGOCOCCAL INFECTIONS,

WITH SPECIAL REFERENCE TO VACCINE TREATMENT.

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(A Report to the Medical Research Committee.)

THE vaccine treatment of many infective conditions, more especially of chronic infections, has now become a widely practised therapeutic procedure. It is a firmly established and well-known fact that a vaccine on injection into the tissues acts like all antigens do in stimulating the production of specific antibodies in the body tissues and fluids of the injected individual. Not only can the presence of these specific antibodies—whether bacteriolytic, agglutinating, complement-fixing, or opsonic—be readily recognised in the blood serum, but by the exercise of the appropriate technique their amounts can be determined with great accuracy. Certain of these methods, indeed, have now become the commonplace procedures of the clinical laboratory, being in daily use for the detection and differential diagnosis of many infective diseases.

There is also some evidence to show that these specific antibodies are not confined to the blood, but may also be found in the other body fluids, more particularly the lymph. An exhaustive investigation into their presence and abundance in various other body fluids, such as the cerebro-spinal fluid, the aqueous humour, the lacrimal fluid, ascitic, pleural, and pericardial fluids, and in various transudates and exudates, would probably throw much light on the exact seat of origin of these bodies.

The question of the presence or absence of these antibodies in the cerebro-spinal fluid becomes an important one in the consideration of the vaccine treatment—prophylactic or curative—of meningococcal cerebro-spinal meningitis, for unless the antibodies reach the interior of the thecal sac, and so be present in the cerebro-spinal fluid, the indications for the exhibition of the vaccine injected subcutaneously would be lacking.

Vaccines have already been administered in this condition, either alone or as an adjunct to other methods of treatment, but according to the official report of the Medical Research Committee on Cerebro-spinal Meningitis no very satisfactory clinical results have been recorded, and so no very definite indications or contra-indications for or against their use can be obtained on clinical grounds alone.

The opportunity of investigating this question experimentally was presented to me whilst working in the London District Cerebro-spinal Fever Laboratory at the Royal Army Medical College at Millbank last year in association with Captain Arthur Davies, R.A.M.C., who suggested this investigation to me, while Lieutenant-Colonel Mervyn Gordon, R.A.M.C., kindly supplied the materials employed.

Young rabbits of 1000 to 1500 grammes weight were inoculated with gradually increasing doses of meningococcus cultures until the blood serum showed a high grade of agglutination towards the strain of the organism injected, several different strains of the meningococcus being employed in the various experiments. The animals were then bled, the serum being employed by Lieutenant-Colonel Gordon¹ in the agglutination and absorption experiments, which proved that four chief strains or types of meningococcus were responsible for the cases of cerebro-spinal fever met with in this country.

The animals, along with a little of their sera and a culture of the infecting organisms, were then handed over to me. The cerebro-spinal fluid was obtained by puncture of the spinal theca through the occipito-atlantoid ligament, where spinal puncture is most easily performed in the rabbit. In some cases blood-stained fluid was obtained. This was at once rejected and only cerebro-spinal fluid free from any trace of blood was employed.

The agglutination titre of the blood and of the cerebro-spinal fluid was then ascertained, the macroscopic method of agglutination being employed. A suspension of a 24-hour culture of the injected coccus in normal saline solution heated to 65° C. for 30 minutes was employed, the heating being employed not only to kill the micro-organisms but also to inactivate the autolysin, for it has been shown by

Raymond Koch that such a heated suspension of meningococci keeps well and gives reliable results for many months. The results were read off after 24 to 48 hours as recommended by Kutscher. The results obtained are set forth in the following table:—

Table Showing Agglutination Titre of Serum and Absence of Agglutinins in Cerebro-spinal Fluid of Rabbits Injected with Various Types of Meningococcus.

Expt.	Type of meningococcus injected.	Agglutination titre of serum.	Agglutination titre of cerebro-spinal fluid.
1.	Carter, Type I.	1 in 320.	Nil.
2.	Chase, Type III.	1 in 320.	„
3.	Shore, Type III.	1 in 256.	„
4.	McPhail, Type II.	1 in 256.	„
5.	Uninoculated control.	Nil.	„

The results obtained in these experiments show that although the serum of the injected animals exhibited a fairly high agglutination titre against the homologous types of meningococcus, the cerebro-spinal fluid in all cases showed no trace of agglutinating properties.

Hitherto very few investigations have been carried out on the antibody content of the cerebro-spinal fluid and these chiefly with *B. typhosus*.

Thus Rosenberg² studied the concentration of typhoid agglutinins in the body fluids of rabbits immunised against the typhoid bacillus. He found that the concentration of the agglutinins depends on their concentration in the blood, and that ascitic fluid and pleuritic and pericardial fluids contain a greater percentage of agglutinins than do cerebro-spinal fluid, aqueous humour, and urine.

Braude and Carlson³ have shown that the serum, thoracic lymph, neck lymph, and pericardial fluid of normal dogs contain agglutinins for the typhoid bacillus, being most abundant in the serum, whilst the cerebro-spinal fluid and the aqueous humour possess no agglutinating properties. In dogs immunised against typhoid bacilli, however, they found that agglutinins were present even in considerable quantity both in the cerebro-spinal fluid and the aqueous humour.

Hughes and Carlson⁴ investigated the hæmolytic power of the body fluids of normal dogs and found that although the serum of the dog is hæmolytic to rabbits' erythrocytes, no laking of rabbits' corpuscles was produced by the cerebro-spinal fluid of any of the 15 dogs investigated.

Working with human body fluids Pick⁵ and Levy and Geissler⁶ have described the presence of bacterio-agglutinins in the cerebro-spinal fluid and aqueous humour, pericardial fluid, and various exudates and transudates in patients suffering from typhoid infections.

Kohler⁷ also found agglutinins present in the cerebro-spinal fluid of one out of a total of ten typhoid patients, whereas the same observer records the presence of agglutinins in the blood of non-typhoid patients as well as healthy individuals to the extent of 15 per cent. of the subjects investigated. It would thus appear that the agglutinins encountered by Kohler were not specific typhoid agglutinins.

The work of Cavazzini,⁸ Capalletti,⁹ Petit and Girard,¹⁰ Meek,¹¹ and Dixon and Halliburton¹² seems to show that the cerebro-spinal fluid is formed, in part if not entirely, by the secretory activity of the epithelial cells of the choroid plexus, which Mott¹³ speaks of as the "choroid gland." Extracts of this body stimulate the secretion of the cerebro-spinal fluid, whereas the quantity of this fluid is not affected by lymphagogues, but is increased by pilocarpine and checked by atropine, and after the injection of pilocarpine the cells exhibit the typical changes met with in active glands after secretion.

Hence we may conclude from a consideration of these experiments that the weight of evidence goes to prove that bacterial antibodies do not pass over, at least in any quantity, into the cerebro-spinal fluid, and that therefore little benefit can be expected to result from the subcutaneous administration of vaccines in cerebro-spinal meningitis.

I beg to express my indebtedness to Captain Davies and to Lieutenant-Colonel Gordon for suggestions and assistance, and to the Medical Research Committee, under whose auspices this investigation was undertaken.

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The Training of the Disabled Soldier.

THE statement of Mr. BARNES, the Minister of Pensions, which was published in THE LANCET last week, on the provision to be made by the Government for men disabled in the war was not made too soon; it was much expected, and will be welcomed by all interested in the care of the war cripple. The War Office, said Mr. BARNES, has undertaken to retain the disabled man as an in-patient so long as there is accommodation for him, and during this time to provide him with manual curative treatment, or, in other words, trade workshops. In order that the Pensions Ministry may get in touch with the disabled man during his period in hospital, Mr. BARNES has adopted the scheme of the Disabled Soldiers Aid Committee, the voluntary body which for some time past has sent representatives to the various London military hospitals to interview the men before their discharge with a view to helping them to find training in skilled trades and subsequent remunerative employment. This visiting will now, therefore, become a general routine throughout the country and be done by members of the local War Pensions &c. Statutory Committees. After discharge from hospital the War Office has accepted responsibility for the man's further treatment as an out-patient in his own district; failure to accept such treatment will subject the man to the risk of losing half his pension, while the discharged man who trains for a new or more skilled occupation will have the inducement of receiving, in addition to his full pension and allowances, free tuition and a small bonus.

This marks a great advance, but it cannot be said that the scheme, as at present outlined, affords a complete solution of the existing difficulties. One of these, which has been experienced by the military authorities in all combatant countries, is to induce the convalescent men to attend the curative workshops where these exist. In the Hammersmith Military Orthopædic Hospital this difficulty has been solved to a considerable extent by the granting or withholding of the special privileges which appeal to the soldier's mind, such as the wearing of khaki in place of hospital blue and the award of extra leave. Unfortunately, the limbless man does not respond in the same way to these attractions and some other suasion must be applied—a matter for the military authorities rather than the Pensions Ministry to devise. A more concrete difficulty is in regard to the provision of training facilities. It is, of course, possible to provide training in a trade at an existing local technical school or polytechnic, and at the same time

medical treatment at another local institution; but it is evident that much effort will be required to coördinate the two, and the cripple will inevitably lose more time each day than if treatment and training were provided under the same roof. At present, too, there is little indication that the local technical institutions are in a position to provide adequate facilities for training except perhaps in the largest centres of population, where, and where only, the different groups of disabled men are sufficiently represented to form classes in the various subjects.

In the direction of continued in-patient treatment, with all its attendant advantages, a promise of better things may be read into Mr. BARNES'S announcement of the formation of a committee directly responsible to the Ministry of Pensions and charged with the task of providing institutional treatment for disabled soldiers after their discharge. The first of these residential institutions which is now approaching completion will deal with a hundred neurasthenics, with whom are to be associated half the number of men who have lost a limb or the use of a limb, the admixture of patients who have only or mainly physical ills to contend with being designed to relieve the mental atmosphere. We may reasonably expect that adequate workshop accommodation is being provided, and that this institution will be the forerunner of others scattered over the country. As the element of treatment is still the most important one in these residential institutions, we cannot help expressing some surprise that Mr. BARNES, in enumerating the personnel of his advisory committee, did not mention the existence of a medical member upon it. There must surely be some officer of a Command Depôt with the necessary experience and administrative ability to qualify for this position. When the advisory committee has done its work we need no longer fear comparison with the French *écoles professionnelles* and the agricultural schools in that country for disabled men. At present, although generous financial provision has been made, the provision of technical re-education of the wounded in this country is below the level of that provided by continental nations, enemy and allied.

Plastic Surgery of the Face.

THE war has afforded sad but great opportunities for the display of surgical skill in the refashioning of the face, and two articles in the present issue of THE LANCET—one by Mr. PERCIVAL COLE and the other by Captain H. D. GILLIES and Captain L. A. B. KING—will serve to show how much may be done by well-directed knowledge and skill in the obliteration of the ravages produced by weapons of war. It was natural that the face should be the region where plastic surgery should first gain successes, for inevitably it would be in this region that the earliest attempts would be made. The classic labours of TAGLIACOZZI were mainly directed to the replacing of noses and lips which had been removed either by injury or by disease. The results of operative interference were here, on the whole, disappointing. In India