The Bacillus Paralyticans.

By GEO. SCOTT WILLIAMSON, L.R.C.P. & S.Edin., Pathologist to the West Riding Asylum, Wakefield.

THIS research was undertaken to establish, as far as possible, Drs. Ford Robertson's and McRae's ætiological hypothesis for general paralysis of the insane. It is hardly necessary to emphasise the importance of giving the fullest consideration to this theory, being, as it is, the first serious attempt of its kind to bring mental disturbance into the category of physical disease, to establish the wealth of histological observation in its place as an effect, and to break from the bugbear of metaphysics and perversion of psychic function. I should like to make it clear that though this research may controvert the ætiological significance of the bacilli of Ford Robertson, it in no wise attacks the fundamental theory of a toxic cause acting through the very definite channels of infection established by Drs. Orr and Rows.

TABLE I.—*Biochemical Reactions of Diphtheroids, giving the Serum Reactions of Infection.*

	K.L.B.[1]	Hoffmann.	Xerosis.	Septus.	Pseudo.	No. 2.	No. 3.	Milk.	No. 2.	*Paralyticans X.*	*Bacillus B.*
Litmus											
Glucose	+	−	+	+	+	+	−	−	+	+	+
Lævulose	−	−	−	−	−	−	−	−	−	−	−
Galactose	−	−	−	−	−	−	−	−	−	−	−
Lactose	−	−	−	+	−	−	−	−	+	±	−
Maltose	+	−	−	−	−	−	+	−	−	−	−
Saccharose	−	−	+	+	−	+	−	−	−	+	−
Raffinose	−	−	+	+	−	−	−	−	+	−	−
Arabinose	−	−	−	+	−	−	−	−	+	−	−
Dextrin	±	−	+	−	−	+	−	−	+	−	−
Inulin	−	−	−	−	−	−	−	−	+		
Glycogen	−	−	−	−	−	−	−	−	−		
Salicin	−	−	−	−	+	+	−	−	−		
Amygdalin	−	−	−	−	−	−	−	−	−		
Glycerine	−	−	+	−	+	+	+	−	−		
Mannit	−	−	−	−	−	−	−	−	−		
Dulcit	−	−	+	−	−	−	+	−	−		
Sorbit	−	−	−	−	−	−	−	−	−		
Arabin	−	−	−	−	−	−	−	−	−		
Milk	−	−	−	+	−	−	−	+	+		

[1] K.L.B. gives very rarely a positive with salicin and glycerine.

https://doi.org/10.1192/bjp.55.231.642 Published online by Cambridge University Press

I have encountered organisms having the morphological and biochemical features of the *paralyticans* in 100 out of 532 cases examined, and in about 730 bacteriological examinations during two and a half years.

The above table illustrates the biochemical reactions of the various members of the group. With carefully prepared media the reactions are most constant. The tests were applied immediately after isolation in pure culture. The bacillus described by Ford Robertson as *Paralyticans brevis* is the commoner organism, about 60 *per cent.* of the *paralyticans* type. The general diseases in which the bacilli were found include the most diverse conditions; in eleven of these the organisms were obtained in a pure condition in the initial blood-serum plating. These eleven cases include:

Post-partum fever, 1; infective endocarditis, 1; sinus in the bladder, 1; sinus in the thigh, 1; pustular acne, 3; cystitis with oxaluria (from the urine), 4.

In 59 cases the organism was associated with others, more especially the other diphtheroids, staphylococcus, streptococcus, coliform bacilli, pneumonococcus, and *Micrococcus catarrhalis*. The cases include:

Acute nasal catarrh, 11; chronic septic vaginitis, 8; urethritis, chronic, 7; pustular acne, 5; septic sinuses, 5; chronic middle-ear disease, 3; hypertrophic rhinitis, 3; atrophic rhinitis, 2; infective endocarditis, 2; rheumatic arthritis, 2; post-partum uterine sepsis; and 1 each of chronic endometritis, chronic parotitis, perirectal abscess, antral disease, lateral sinus thrombosis, sub-diaphragmatic abscess, necrosis of bladder-wall, eczema, and keratitis punctata.

In addition to the above, the bacilli have been found in 10 tubercular sputa, in 3 urines, and in 17 throat swabs taken for diphtheria, and 3 times in fæces.

In general paralysis, the insanities and the controls, the bacilli were obtained only once in pure culture, and that from the cerebro-spinal fluid from a case of secondary dementia dead from tuberculosis.

The figures make it plain that—(1) these bacilli are not at all uncommonly found on the normal body, and suggest the possibility of a definite pathogenic function; (2) that the paralytic type of diphtheroid increases with any increase of the group as a whole; (3) that institution cases, normal and diseased, more

readily yield the bacilli in culture, but not more so than the diphtheroid group as a whole; (4) that what may appear at first sight to be an increased prevalence in general paralysis is but an indication of the general increase of the group in institution cases, *i.e.*, though the curve of incidence for general paralysis

TABLE II.—*Table of Percentages for Comparative Purposes (not Statistical).*

	Number of cases.	Type of diphtheroid.					Number of examinations.
		Paralyticans.	Hoffman.	Xerosis.	Others.	Group.	
		Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	
General diseases .	422	16·5	21	12·5	3	45·5	422
General paralytics .	44	23	41	9	4	57	63
Normal persons .	58	21	42	7	7	54	76
Other insanities .	42	19	41	7	0	57	42
Attendants . .	16	31	50	25	12	75	27

TABLE III.—*Table to show the Total Diphtheroid Numbers and the Number of Each Type.*

	Number of cases.	Source of material.	Number of cases yielding diphtheroids.					Other organisms.	Pure culture.
			Paralyticans.	Hoffman.	Xerosis.	Others.	Group.		
General paralysis of the insane .	21	Throat .	3	7	3	—	11	21	—
	21	Skin . .	8	8	3	3	18	21	—
	21	Blood .	2	3	—	—	4	8	—
	21	C.S.F. life .	1	2	—	—	3	7	—
	23	C.S.F. P.M.	4	6	1	2	7	22	—
Normal persons .	38	Throat .	5	13	2	3	21	38	—
	38	Skin . .	6	14	5	4	21	38	—
	15	Blood .	—	3	1	—	3	5	—
	10	C.S.F. life .	—	1	2	1	3	4	—
	24	C.S.F. P.M.	3	5	1	3	8	24	—
Other insanities .	8	Throat .	8	2	5	—	5	8	—
	15	Skin . .	5	6	2	—	10	15	—
	22	C.S.F. life .	3	5	3	—	6	11	—
	34	C.S.F. P.M.	4	7	—	—	7	27	1
Attendants . .	11	Throat .	3	8	4	2	11	11	—
	16	Skin . .	4	7	4	—	10	16	—

Normal persons meaning those free from any obvious bacterial infection. All C.S.F. obtained within four hours of death.

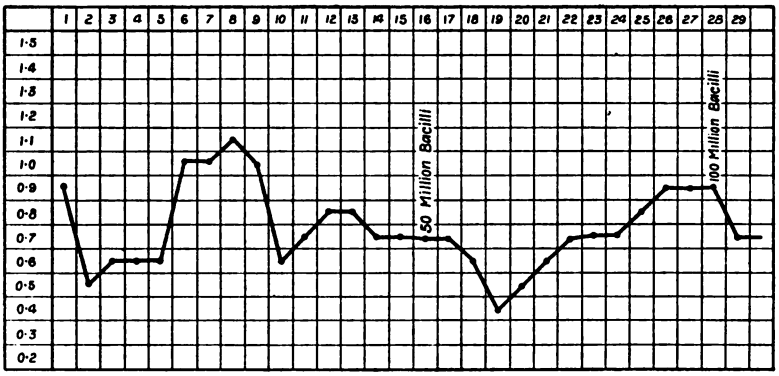
https://doi.org/10.1192/bjp.55.231.642 Published online by Cambridge University Press

would be placed further from the abscissa, the outline of the curve is the same in the normal healthy, institution healthy and diseased.

This increase of a group of organisms in institution cases is no uncommon thing; staphylococci, streptococci, and other organisms will readily afford examples. Nor is the frequency of one type of organism uncommon in institutions—staphylococci, streptococci, coliform bacilli, exhibit this often to a striking degree.

It is generally conceded that, coincident with organismal infection, there is a change in that content of the blood-serum,

CHART I.—*Opsonic Index. B. Paralyticans Brevis (Pure). Case, Acne.*



Type of curve in *paralyticans* infection.

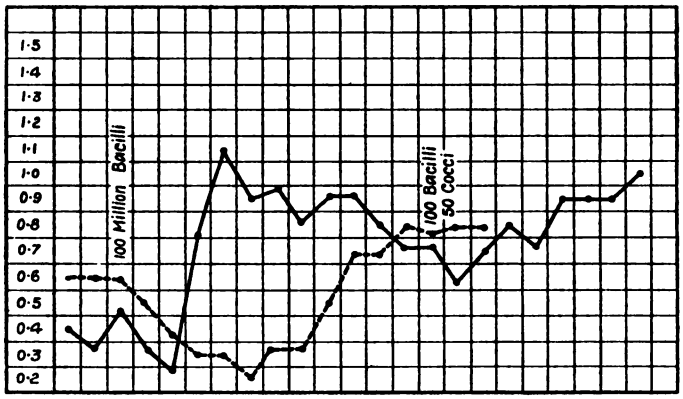
which aids phagocytosis, the so-called opsonin; and that a bacillary infection gives rise to an immune body. In a general way a variation of the opsonic index to an organism may be taken as a guide to infectivity. In the eleven cases of general disease above detailed three only gave an index which could be considered as abnormal.

The opsonic chart shown is typical of these three cases, and is, further, typical of an infection. The fluctuations are generally accounted for by auto-inoculation with bacillary toxin. In the cases of mixed infection thirteen of the fifty-nine gave a similar curve. It is usually possible to steady the opsonic curve by inoculation with the bacilli of infection. The above cases

https://doi.org/10.1192/bjp.55.231.642 Published online by Cambridge University Press

responded readily to such inoculation. It may be taken, then, that these organisms can be infective, and as such can cause a rise or fall in the opsonic index. In general paralysis only one such case occurred, having the index curve shown ; the patient was suffering from acne spread over the legs and thighs, yielding a staphylococcus and *Bacillus xerosis*. On the same chart the general curve of indices to six other strains of the organisms is shown. Though an ultimate response to inoculation with the autogenous organism does occur, it is slower in the rise, but corresponds with an established improvement ; the members of the group can aid in steadying the opsonic curve. This

CHART II.—*Opsonic Index. B. Paralyticans Longus. Case, General Paralysis with Acne.*



..... Opsonic index to other strains.

suggests the group reactions of agglutinins as fully worked out for the colon-typhoid group. In the other general paralytics the index is low compared to the normal, the curve approximating a straight line. This subnormal condition also applies to staphylococci, *Bacillus coli*, streptococci, pneumonococci, and to the majority of the commoner pathogenic organisms. The tubercular index is usually about the average normal. These opsonic curves apply to thirteen strains of *B. paralyticans* ; no instance occurred in which a variable index was encountered, apart, of course, from the acne case.

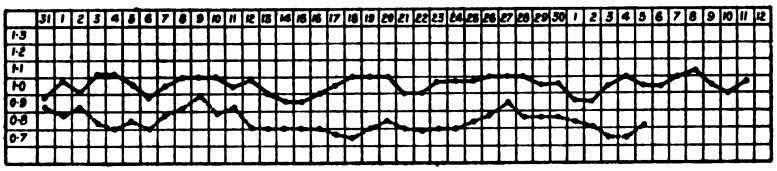
The normal index is from	·93–1·23.
The attendants	·81–1·3.

The general paralytics . . . . . ·78–1·1.
The other insane . . . . . ·75–1·0.

To test the possibility of variation in the serum, injections beginning with 20,000,000 bacilli were given and the index noted; four separate strains and a pooled culture were used in making the vaccines. The response to inoculation is good in

CHART III.—*Opsonic Index. B. Paralyticans Brevis;* 8 *Strains.*

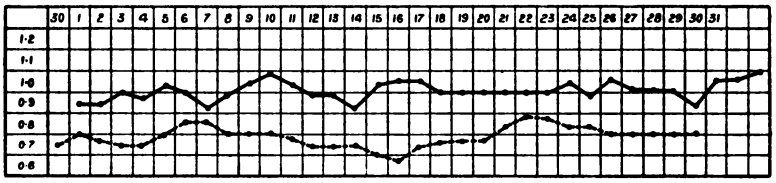
——— Average 54 normals. ·93 to 1·23.



..... Average 20 normal general paralytics.

CHART IV.—*Opsonic Index. B. Paralyticans Longus;* 5 *Strains.*

——— Average 54 normals. ·89 to 1·19.

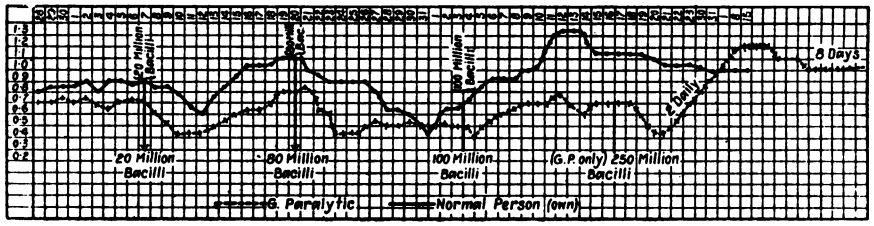


..... Average of 20 normal general paralytics.

general paralysis and insanities, though somewhat quicker in the rise and fall compared to the normal. Injection up to 250,000,000 bacilli maintaining the opsonic index at or about 1·2 and 1·3, creates no improvement in general paralysis nor has any exacerbation in the course of the disease ensued thereon—observations extending over seven months in five cases. By producing a summation of negative phases a very definite fever may result but no exacerbation of any paretic or

other symptoms—three cases. In general paralysis and the insanities there is, then, a lowered resistance to this diphtheroid, and this is in keeping with similar observations on the other diphtheroids, cocci, and other organisms. So far as this opsonic test goes the general paralytic is not in the same category as the cases having a definite infection of a more or less chronic nature, but may be in keeping with the fifty-four cases with normal indices having the organisms present at the seat of infection. It seemed possible, then, that the *B. paralyticans* obeyed no rule as to an opsonic response, while being pathognomonic. This is not a common occurrence in disease, but it is seen in diphtheria and tuberculosis and perhaps some other conditions. In these cases the deviation of the complement test, Bordet-Gengou phenomenon, appeared to be appli-

CHART V.—*Opsonic Index. B. Paralyticans Brevis Vaccine.*

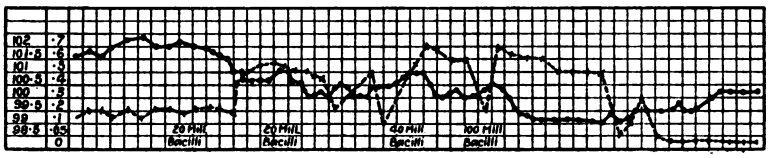


cable. Using the emulsion of the bacilli an an antigen I tested twelve opsonic positives and twelve opsonic negatives among the general diseases, twenty-two general paralytics, ten insanities and five normal persons. All the opsonic positives gave a positive result, *i.e.*, the complement was bound by the antigen and hæmolysis did not occur ; only one other case gave a positive result, and that was the general paralytic with acne, again an opsonic positive. It would appear, then, as far as this test goes, the *B. paralyticans* is not pathognomonic to general paralysis. It may, however, be argued against any such conclusion that other organisms definitely infective do not give this test. Selecting eleven cases of diphtheria I used the autogenous bacilli (free from toxin) as antigen, and found that only one case gave a positive complemental test. Thus diphtheria may be cited as an example of the latter argument.

https://doi.org/10.1192/bjp.55.231.642 Published online by Cambridge University Press

That tubercular disease sometimes fails to give this test is well known. It seemed justifiable to place general paralysis in the same category as diphtheria and tuberculosis as far as the opsonic and the Bordet-Gengou reactions go, always accepting the bacillary hypothesis. It seemed to me very possible that though there was no demonstrable immune body in infections with tubercle bacillus and diphtheria bacillus, there might be an immune body to diphtheria and tuberculosis—that is to say, the antigen was not the bacilli but the product of bacilli and local tissues. Acting on this I prepared an emulsion of tubercular liver and kidney and of diphtheritic membrane, filtered both through a Chamberland candle, and used these as the antigen. Selecting nine cases of tuberculosis (six of them caries, two tubercular lupus, and one phthisis)

CHART VI.—*Induced Low Index. B. Paralyticans Brevis and Longus Vaccine.*



..... Temperature.

which gave negative complemental tests by the usual method, and five cases of diphtheria of the same type, I applied the test, using the new antigen, with positive results in every case. One control, a case of scarlet fever, gave a positive result. The other controls were—two cases of pneumonia, three of scarlet fever, one Bright's disease, one typhoid, one of hydatid disease, and eight normal bloods. Without venturing an opinion as to the specificity of this reaction in the above diseases I thought it comparable with the *paralyticans* in general paralysis, since it seemed to prove that an antigen can be produced at the seat of disease apart from the organism itself. The antigen *paralyticans* was made from uterine scrapings from the opsonic positive case of uterine disease giving a pure culture of the bacillus. This antigen gave positive results in twelve cases, positive by the ordinary method and also opsonic

positive. It gave negative results with six normal sera, ten general paralytics and thirteen insanities. The case of acne in general paralysis was not tested. In this general paralysis is unlike diphtheria and tuberculosis.

The next step was to use an emulsion of nervous tissue of general paralysis as an antigen. Three typical brains were used as this antigen. While general paralysis serum gave positive results in seventeen out of twenty-two cases of general paralysis, no positives occurred in any of the cases in which these serum reactions had proven a definite infectivity. Thus the antigen body in the brain of general paralysis, if such it is, is not the same as the antigen of the *Bacillus paralyticans* in true infections. In conclusion, I would state that time has not permitted the including of the details of controls, but these controls covered every possible source of error.

To summarise, it may be taken as proven that bacilli having the characteristics of Drs. Ford Robertson's and McRae's paralytica type do exist.

That they are widely distributed, and would appear to be of the common organism of the normal skin and throat.

That they can give rise to disease.

That the disease is generally of a chronic type.

That these bacilli disturb the opsonic content of the blood serum.

That they produce an immune body.

That they can act as an antigen.

That an antigen may also be produced at the seat of disease.

That the blood-serum of the person infected by these bacilli does give the serum responses typical of bacillary infections.

That the general paralytic can give all the above tests in response to artificial and natural infection with the *Bacillus paralyticans*, but does not.

That while the bacilli of Drs. Ford Robertson and McRae may be a considerable factor in the secondary infections of many general paralytics it is not alone in this respect, but only presents a peculiarity of the diphtheroid group as a whole, and that in common with other organisms, of flourishing where there is a lowered resistance.

That the establishing of a special neurotoxicity for the bacilli is not a complete argument for its specificity in general paralysis of the insane.

Discussion,

At the Annual Meeting held at Wakefield, July, 1909.

Dr. W. Ford Robertson said that he desired, in the first place, to acknowledge the extraordinary courtesy Dr. Williamson had shown in sending him, a few days ago, a copy of his paper. One must recognise the vast amount of labour that these observations had entailed. It was something at least to be regarded with satisfaction that Dr. Williamson had been able to confirm the existence of these special types of diphtheroid bacilli, for there were other "competent bacteriologists" who had been unable to do so. The paper was, however, obviously intended to be a very serious attack upon the position maintained by his colleagues and himself, and as such it must be dealt with. He thought that Dr. Williamson had laid himself open to adverse criticism at many points. It was a fundamental error to have slumped the various bacteriological examinations as had been done, for the isolation of these special bacilli from a mucous surface that normally harboured micro-organisms was of comparatively trivial importance. A totally different significance was to be attached to the isolation of these bacilli from the cerebro-spinal fluid or blood during life. He and his co-workers had fully recognised the wide distribution of these bacilli upon mucous membranes, and their occurrence in persons who did not suffer from general paralysis. What they maintained was, that certain highly virulent strains of these bacilli were handed on, generally venereally, and that, when in this way they reached susceptible persons, they invaded the tissues and infected the central nervous system, and so produced general paralysis. Whether this infection was always an organismal infection, or might sometimes be only a toxic infection, was an open question. These facts and distinctions received no recognition from Dr. Williamson. It was further unfortunate that the virulence of the bacilli isolated could not be tested. They had attached importance to bacilli which were virulent to mice, though it was true that all strains did not manifest this character. But as a matter of fact they never regarded any of these bacilli as important unless they were proved to be virulent to mice, or there was evidence that they were invading the patient. Many of the strains isolated by Dr. Williamson in control cases might have been of little virulence, and therefore unable to invade the tissues. Again, it was not the case that they had attributed exclusive importance to those two strains of diphtheroid bacilli. They had left it an open question whether or not other micro-organisms with similar pathogenic powers produced general paralysis. They had also attached importance to secondary infections. The tabulation of results from normal persons was to his mind incredible. There was something wrong here, which indirectly affected one's trust in the other results recorded. With regard to the cases termed "other insanities," there was no proof that some of them might not have been early cases of general paralysis. Besides, they had fully recognised that the pathogenic action of these bacilli covered a much wider field than that of general paralysis. In general paralysis there was simply the special fact of a cerebral infection, either micro-organismal or toxic. His results with opsonic tests were just the converse of those recorded by Dr. O'Brien, who constantly obtained opsonic responses, and who had found that there were continual fluctuations in the opsonic index towards these bacilli in cases of general paralysis. Dr. O'Brien had the immense advantage that he had obtained a series of excellent therapeutic results by the use of vaccine treatment under the guidance of the opsonic index. Dr. Williamson had admitted the uncertainty of the application of these opsonic tests in this investigation, and yet he made very far-reaching generalisations from his results. He had likewise admitted that the deviation of the complement test might not be applicable in general paralysis if the special bacilli were used as the antigen. He had, further, when he used general paralytic's brain as the antigen, obtained a deviation of the complement in seventeen out of twenty-two cases of general paralysis. This was a remarkable result, and one probably of much greater importance than the observer attributed to it. Indeed, he had tried to minimise its importance by saying that "no positives occurred in any of the cases in which the above serum reactions had proven a definite infection with the *paralyticans* types." Apart from the question of the value of the alleged proof of such definite

infection, it was to be pointed out that he was failing to make a distinction between cases in which there was a simple infective focus in a mucous membrane and those in which there was cerebral infection with destruction of nervous tissues. They at least had made such a distinction, and had recognised that there were very many persons who were defending themselves against the local attack of these special bacilli without suffering from general paralysis. For these tests to have any precise value it would be necessary to study them in animals artificially immunised with these micro-organisms, and in others in which a chronic infection of the nervous system had been produced. Much of the evidence that Dr. Williamson had brought forward was of very uncertain interpretation, and he was, the speaker thought, very far from having established his contention that his results controverted the ætiological significance of these diphtheroid bacilli. The evidence to which they attached special importance remained untouched, and it was a curious fact that Dr. Williamson had not alluded to a single item of it in a paper which professed to be an attack upon their position.

Dr. WILLIAMSON asked permission to reply to Dr. Ford Robertson at once. Dr. Robertson brought forward the question of virulence. It was a very well-known thing in bacteriology that animals could not give evidence of virulence and be compared with human beings in any and every bacteriological infection. There were certain organisms which were very virulent indeed to some animals but not at all virulent to guinea-pigs, so much so that unless the virulence of the diphtheria bacillus had been proved by its source, the mere use of the guinea-pig and the fact of the guinea-pig dying therefrom did not give an indication of virulence; it simply showed the virulence to the guinea-pig. All the immuno-chemistry which had been done went to prove the fundamental differences between sera of the guinea-pig and sera of the human being. The probability was that those immune responses in sera were directly derived from the type of bacilli which were circulating in the blood, be it guinea-pig or human being. The habitat of certain organisms was peculiarly human. Consequently one would say that the virulence, as far as guinea-pigs was concerned, was a considerable evidence as establishing Dr. Ford Robertson's hypothesis as to the toxicity, but it was not a justifiable argument for the ætiology of the bacillus as applied to general paralysis. But he did maintain that the opsonic tests and the deviation of complement tests were tests of virulence; they proved the virulence of diphtheroid bacilli as to whether or not they could produce disease in human beings, and the great point was that concerning human beings. His opsonic tests showed him that those organisms could give rise to disease. And as far as he had gone in investigating general paralysis —he admitted he had only done twenty-two cases—looking at it peculiarly from the point of view of the opsonins and the immuno-chemistry, he could see no reason for ascribing to the bacillus a special virulence in connection with general paralysis. With regard to the infection being peculiar to nerve-tissues, and the point made by Dr. Robertson that an excellent medium for the establishment of an antigen would be the brain of a person, that might be so; but there were all sorts of organisms, growing in different situations in the body, which would certainly get an enhanced virulence for the central nervous system. One had only to pass an organism into two or three animals to get this virulence increased. One could almost get specificity established by constantly passing it through one strain of animal. With regard to the brain of the general paralytic, he thought Dr. Ford Robertson began by assuming that his diphtheroid bacillus was in the brains of general paralytics, but when Dr. Robertson recommended to him that because a general paralytic brain gave a specific reaction with general paralytic sera, that meant that the diphtheroid bacillus was there, he would reply that it meant nothing more than that the general paralytic might be the result of one type of infection, and that much was already admitted. He agreed with Dr. Ford Robertson in the point, that general paralysis might be one type of an infection. But one could not argue that because in the brain of a general paralytic the antigen was specific to general paralysis, that the specificity of the antigen depended on any bacterial content. It was a rare thing to find bacteria in the brain of a general paralytic in his experience, which amounted to eighteen *post-mortems*. At the moment he did not recall any other questions which Dr. Ford Robertson alluded to to which he had not replied.

Dr. WINIFRED MUIRHEAD said she desired to refer to her own observations in

connection with insanity. She had been working at the blood and cerebro-spinal fluid of general paralysis. She always got the blood during the seizure. If necessary an anæsthetic was given when obtaining the cerebro-spinal fluid, and that also was obtained during the seizure. In twenty-five cases of general paralysis ante-mortem, she isolated a diphtheroid organism from the blood in eight cases, or 32 *per cent.* In three of the same cases she got the diphtheroid bacillus in the cerebro-spinal fluid, or 12 *per cent.* In three of the eight cases she reduplicated her results twice from the blood, and in one case three times from the blood. *Post-mortem*, in twenty-seven cases of general paralysis, in eight, or 29·6 *per cent.*, she got an identical diphtheroid bacillus from the cerebro-spinal fluid in pure culture; in one case of these only from the blood in pure culture. Fifteen of these twenty-seven cases were examined also during life, five being positive to that special type of diphtheroid, and in one of these five cases, *post-mortem*, she did not get this diphtheroid type at all, but a coarsely growing diphtheroid, which was associated with another bacillus. It was not a pure incubation from the cerebro-spinal fluid. To summarise, out of fifty-two cases of general paralysis, ante-mortem and *post-mortem*, she isolated an identical diphtheroid in sixteen, or 30·7 *per cent.* Five of those general paralytics were females, and in only one did she succeed in isolating that or any organism from the blood and cerebro-spinal fluid. It was the organism under discussion, and was obtained *post-mortem* from the cerebro-spinal fluid in pure culture. She was pregnant, and was confined at eight months. The child lived only a few hours, and showed no signs of congenital syphilis. There was no invasion of organisms in the child, and microscopical sections showed an ordinary typical fœtal brain. The appearances, both microscopical and macroscopical, of the mother were typically those of general paralysis. She had twenty-nine controls of other types of insanity. She isolated the identical bacillus from the blood in seven out of twenty cases of acute delirious insanity, and those patients were all extremely ill; one came in almost moribund. One was post-rheumatic; a child, æt. 16, who was sent to them from another infirmary while delirious, and who had marked chorea. It was not thought that the child would live more than a few hours. Blood was withdrawn immediately, and in that blood the organisms were mixed; the type of diphtheroid organism under discussion, and a delicately growing coccus, which she lost before she could cultivate; she thought it might be the *Micrococcus rheumaticus*. Of the seven cases of delirious insanity only one died, and in that case a *post-mortem* was not allowed; that is, from twenty cases of extremely acute delirious insanity, in seven, from the blood withdrawn shortly after admission when the patients were acutely ill, with a temperature above normal in some cases and subnormal in others, and with a rapid pulse, she got the identical diphtheroid which she isolated in general paralysis of the insane during a seizure. One of the twenty-nine cases was that of a man about fifty-five to sixty years of age, who was clinically like a case of general paralysis, and was diagnosed as such. He was restless and going downhill rapidly; he also had delusions, etc. He was too restless to permit of lumbar puncture being done, except under an anæsthetic. When it was performed there was a tremendous excess of pressure, which was accounted for by the fact that he was a man with a high-tension pulse and thickened arteries, but there was no lymphocytosis in the cerebro-spinal fluid, and it did not respond to any of the chemical tests for general paralysis. She was not doing the Wasserman reaction at that time. From that man's blood, taken at the same time, she got a streptothrix—a delicately growing one. Three months later he developed hæmatoma auris, and she isolated a streptothrix from this fluid associated with Hoffmann's diphtheroid. That man died six months later, and from the cerebro-spinal fluid, in pure culture, she got a streptothrix. It was interesting to have obtained the streptothrix three times. With regard to the opsonic index her results in that respect had been very variable. The vaccine treatment of the general paralytics, from whom she had isolated the organism, with their own organism gave no result; no apparent improvement occurred in the patient. And even the opsonic index she was not satisfied with; it was not such a clearly-defined index as with the staphylococcus and streptococcus. One very interesting thing about the vaccines was that in one case, a general paralytic, she used a very large dose of his own vaccine. The man became acutely excited, and had a marked rise of temperature; he was very dirty in his habits, and

altogether very confused, and went rapidly downhill. He recovered quickly. The pathogenicity was very slight. Out of thirteen different strains of that type of bacillus she found five strains slightly pathogenic to mice; never to guinea-pigs or to rabbits. In the first case in which she recovered it she inoculated the blood directly into two mice, and six days later she killed one of the mice and recovered the organism from the spleen. A fortnight later the other mouse died, with paralysis on one side of the body. The conclusion she had formed was that this diphtheroid bacillus was not the cause of general paralysis of the insane and delirious insanity. The incidence of syphilis could not be ignored in general paralysis, but in delirous insanity it was a negligible quantity. If syphilis had the power to determine the characteristic symptoms present in no other type of insanity, one must assign the predisposing cause in general paralysis a far more important *rôle* than the diphtheroids, if one assumed that they were a cause of general paralysis. The secondary conclusion at which she had arrived was that it must be determined whether it was an aggravating concomitant or of no importance. In the case of the child with post-rheumatic delirious insanity there was a mixed infection. There was the delicately growing type of coccus, which showed that the resistance of the individual must be very much lowered to have a double invasion like that. Then, also, in the case of excited dementia the man, aged about sixty, rapidly progressed, and there again in the blood there was a streptothrix and a coccus. One was inclined to think from that that the resistance of those patients must be very low, and that in consequence the invasion by organisms of low pathogenicity was fairly easy. One point which might be raised was: Was that diphtheroid any special type of neurotoxin? Why should one be able to get it in delirous insanity and in general paralysis of the insane? Had it some special affinity for the central nervous system? The cases she had referred to were certainly extremely ill, and one died in five weeks. She did not yet know what conclusion to form, whether it was of no importance, or whether it was important. But, as far as she had gone, she did not feel justified in saying it was a cause of general paralysis of the insane, because it occurred also in another insanity where the patients were just as acutely ill as the general paralytics.

Dr. McRae said he had listened very carefully to Dr. Williamson's paper, and he was intensely interested in it. He did not feel prepared at the moment to criticise it, but he felt it was only right to refer to one point of great importance in the work of Dr. Ford Robertson and himself. Whenever the serum was found to give no reaction in general paralytics, they examined their organism and found it was not virulent. Immediately they recovered the organism in virulent form as tested on mice, reactions after injection occurred once more clinically.

Dr. Williamson replied that their virulence referred only to mice, and Drs. Robertson and McRae drew from that the conclusion that because a serum was of no avail before the virulence was raised, that this virulence to mice meant a virulence to the human body.

Dr. Ford Robertson said it was not considered unjustifiable in immunising horses to produce a diphtheria serum, so why should it be considered unjustifiable in their case? The two cases were exactly parallel. One would not think of using a strain of diphtheria bacillus which would not kill a guinea-pig.

Dr. Williamson replied: One of the organisms used in the Lister Institute to produce serum was one of low pathogenicity to guinea-pigs, yet it could produce such a degree of disturbance in the horse as to justify its use. The serum had a high protective power against virulent diphtheria in guinea-pigs.

Dr. Ford Robertson said that represented an advance which he was not aware of.

Dr. McRae said that by the use of that serum, which they believed to have a potency because virulent organisms had been passed through the sheep, they considered they did reproduce or exaggerate the symptoms of general paralysis. That was controlled by several cases by using anti-streptococcic and anti-diphtheritic and other sera, but they had no effect at all, either in producing an exacerbation, or in lowering any temperature which already existed. With regard to Dr. Muirhead's cases of acute delirious mania, he did not think all were so positive in diagnosing general paralysis. He did not think one could exclude those acute delirious manias from the possibility of general paralysis. Acute delirious conditions were met with in general paralysis. Advanced cases sometimes came into the asylum

which died in a few weeks. He did not think it was always easy to exclude general paralysis.

Dr. MUIRHEAD said that of the cases of delirious insanity from which she isolated the organism, lumbar puncture was performed in all, but leucocytosis was not found in any; neither did any of them give the chemical tests or Wasserman. Several of the cases were comparatively young women, most of them being under twenty.

Dr. MCRAE rejoined that he had had cases die of general paralysis under twenty years of age.

Dr. WILLIAMSON, in further reply on the discussion, desired to thank all who had spoken for the spirit in which they had received his work which was set out in the paper. He thought the best thing to do was simply to say he left the paper on the table. He did not think he could adequately sum up the various arguments which had been used. Dr. Ford Robertson and he had not agreed with one another, but he would like to state that in the position in which Dr. Ford Robertson had put the *Bacillus paralyticans* he, Dr. Williamson, put secondary infections, with all and every organism which could be pathogenic to man. And if one went on searching through the insane, or through any individuals whose bodies were not healthy, it would be found that both the fauces and all the natural channels could acquire bacterial flora which were not present in the normal condition. And the patients with general paralysis were peculiarly susceptible to bacillary invasion. He still said that, in his opinion, no single organism would fulfil all the conditions required of it in order to give that organism an ætiological significance. But one could find a certain number of diphtheroids in a certain number of general paralytics who would give all the serum responses of immunity and the opsonic index, but in another institution it was not so. For instance, the organism of general paralytics in Wakefield he would call a Gram-negative coccus. He could isolate it with such frequency from various situations, such as the urine and the blood, and in an epidemic of influenza in Wakefield he got that Gram-negative coccus. Therefore he preferred, under the circumstances, to leave the discussion in that way.

The Cerebro-spinal Fluid in General Paralysis and the Nervous Lues.

By GEO. SCOTT WILLIAMSON, L.R.C.P. & S.Edin., Pathologist to the West Riding Asylum, Wakefield.

I WISH to lay before you the results of an examination of the cerebro-spinal fluid in general paralysis and the nervous lues compared with insanities of almost every type, with a few cases of organic disease other than brain disease, and with ten normal fluids. The most serious difficulty met with in obtaining fluid by lumbar puncture with a view to chemical analysis is the admixture of blood. I may mention that in no instance have I seen any ill-effects on a patient from the withdrawal of the fluid; nor have I noticed any abatement in the acute conditions of general paralysis. The investigation has included the detection of albumose, nucleo-protein, and cholin; the

https://doi.org/10.1192/bjp.55.231.642 Published online by Cambridge University Press