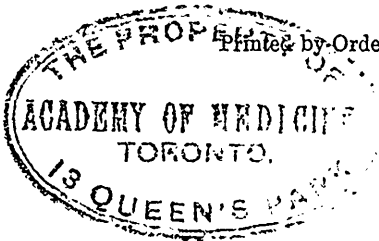


Bulletin
OF THE
Ontario Hospitals for
the Insane

*A Journal devoted
to the interests of
Psychiatry in Ontario*



Printed by Order of the Legislative Assembly.

EDITORS:

C. K. CLARKE, M.D., LL.D.,
ERNEST JONES, M.D., W. C. HERRIMAN, M.B., J. A. CAMPBELL, M.B.

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IMMUNITY AND ANAPHYLAXIS: A CONSIDERA-
TION OF SOME CURRENT PROBLEMS, AND
A NOTE ON SERUM AND VACCINE THE-
RAPY.

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In a recent article Moss (1) in recording his experi-
ences during a year spent in visiting the laboratories of
Europe and England, noted that the activities of the great
majority of the foremost workers in the field of scien-
tific medicine to-day were in studies which might all be
included under the title "Immunity and anaphylaxis." This
is indeed noteworthy and in sharp contrast to what
a student of two or three decades ago would have
found to be the case. At that time Virchow and his
followers in the school of cellular pathology or histo-
pathology dominated the first of laboratory investiga-
tors in medicine, and the hallmark was the ability to
differentiate, to trace and to elucidate pathological devi-
ations in the structure of the various body tissues. In
1908, Ehrlich and Metchnikoff were awarded the Nobel
prize in medicine for having (as was probably conceived

by the council awarding the prizes) together done the most, although working along different paths, to build up a distinct idea in modern medicine. This idea is embodied in the word Immunity, the resistance of the living body to disease processes; or in its narrower, but more common acceptation, to infective agents or their products. Anaphylaxis is the complementary term and means hyper-susceptibility to disease shown under certain circumstances, to be spoken of later.

So we see at the outset that while an exact understanding of the changes that come or are brought about in the cell of the body, is quite as necessary to-day as in the time of Virchow or in the heyday of his school, it is essential that we realize that the path of progress to-day is along lines which have to do with the study and investigation of living, vital processes, not only in their physiological aspects, but also in their pathological physiology. This then being the case, it logically follows that the blood and tissue fluids must of necessity come in for no small amount of consideration and workers in Immunity have charged themselves with this task.

While it will be impossible in a brief summary of this sort to go into many of the very interesting historical aspects of the subject, it is necessary for a clear understanding of the case, to comprehend certain facts that are now considered corner-stones upon which most of our current knowledge rests.

Ehrlich, one of the earliest investigators, and widely recognized as the foremost living exponent of the German school of "humoral" immunity, (Foder, 1887) has perhaps done more than any other single worker to make clear many extremely interesting phenomena. On the other hand Metchnikoff, as the leader of the French school of cellular immunity, by his fascinating studies and extremely logical conceptions, stands almost side

by side with his German contemporary. While a great deal of valuable work has been done both in Great Britain and in America, we would really be anticipating if it were suggested that an English school existed. The pupils and admirers of Sir A. E. Wright have named their chieftain as the logical leader of this school. It would seem that the future must decide this question, in addition to several others.

Since about 1880, work has been progressing in this field, but not until three years later, that is, in 1883, when Metchnikoff announced his theory of phagocytosis, did the wonderful import of the work being done in the new province come home to those engaged in medical research. The man who sponsored the theory was not, and is not, a doctor of medicine, but of philosophy, originally engaged in work along zoological and biological lines. His observations led those in charge of the Institut Pasteur, in Paris, to engage him to work in biological problems in medicine. His first great contribution in this branch was in connection with his work on phagocytosis and his deduction was briefly this, that the white blood cell (polymorphonuclear-microphages and large mononuclear-macrophages) were the scavengers in the blood, or the army of the body which was ever on the alert to resist an invasion of the enemy; that when any inert or harmful agent entered the blood stream these cells were attracted to the spot by an influence spoken of as chemiotaxis (positive when attractive, negative when repellent) and once arrived they engulfed the foreign substance whether it was a harmful agent, such as a bacterium, or merely some non-active substance. It may perhaps be thought curious that the name Pasteur, a master scientist of the French School, has not been earlier mentioned in connection with the activities of that school. This has been with a definite object in view, namely,

that the consideration of his work in a brief *resumé* on the therapeutic applications of discoveries in Immunity may better enable one to realize what may be and has been done to benefit mankind by such studies.

Following Metchnikoff, and working in conjunction with him, came a long line of men now famous wherever scientific medicine is known—Calmette, Roux, Bordet, Nicolle, A. Marie, Levaditi and a host of others, while a brief list of other famous investigators in immunity, German, English, Italian, and American, would include Koch, Morgenroth, C. J. Martin, Nuttall, Maragliano, H. Sachs, Neufeld, Arrhenius, and Madsen, Kraus, Koller, Theobald Smith, Von Pirquet, etc. In the development of the idea of phagocytosis by white cells of the blood, Jules Bordet (2) of the Institut Pasteur, Brussels, did much to make clear many phenomena which were of the utmost practical importance. While it is, and always has been, the contention of the French School that the phagocytes are the fundamental elements in protecting us against the invasion of infective and toxic agents, still it should be remembered, as Bordet has shown, that the substances which are mainly responsible for this protective function, while they are secreted by the phagocytes, may be present in the blood serum. And while phagocytosis is the fundamental factor, this reaction often acts outside the phagocyte and is of material assistance in warding off infections. Büchner described a substance which he spoke of as Alexin, which he found to be present in all sera. It is a thermostable substance which is destroyed by heating for half an hour at 56 degrees C. This alexin he described as the bactericidal element in blood serum. It possesses no specific qualities and renders no greater service in attacking one organism than another. A second substance was described by him, however, to which he gave the name "preventive substance, (or "substance sensibil-

isatrice," sensitizing substance, immune body or antibody) which appeared in the serum after a suitable period, only when an animal had been inoculated with a given micro-organism; and was able, acting in conjunction with the bactericidal substance (alexin), to destroy the infective agent or inhibit its growth. He further found that this preventive substance was specific; this is to say, that on the infection of cholera vibrios, for example, into an experimental animal, the immune serum produced was able, in conjunction with the bactericidal substance (alexin), to act only on the cholera vibrios. His theory of the mechanism of this protective agent was that the bactericidal and preventive substance in some way combined to form a combination which was active against infective agents. As was noted above, the alexin was believed to be the product of the white blood cells, and the preventive substance, something produced in the serum on the introduction of some harmful foreign element. Later it was believed by Bordet and his followers that the preventive substance or immune body in the serum fixed the alexin to the element to be destroyed, thus enabling it to act. This also was Metchnikoff's view, and to this substance he gave the name "*fixateur*." In 1896, working in conjunction with Gengou, Bordet discovered the phenomenon (now known by the name of the Bordet-Gengou reaction of fixation) which has since come into very practical use as will be shown shortly. They demonstrated the fact that if an animal, for instance the rabbit, was infected with the red-blood corpuscles of another animal, for example the sheep, the serum of the injected rabbit acquired the power of destroying the red-blood cell of the sheep in the presence of the third substance. Supposing one had alexin and sheep corpuscles, one could determine by an appropriate mixture whether or not there existed in the blood serum of the rabbit a substance capable of destroying the sheep cor-

puscle. In a like fashion it has been possible to apply this reaction for the determination of the presence or absence of antibodies (or immune bodies) in any unknown sera, provided one has the specific agent necessary for the production of such an antibody plus alexin present in correct proportions. This method of diagnosis has been applied by Wasserman, Neisser, and Bruck in the diagnosis of syphilis and the Parasyphillides Tabes and General Paresis.

In the meantime, Ehrlich had elaborated an hypothesis which is known as the side-chain theory, which is his explanation of how immunity is brought about. He regards the body cell as being composed of a central portion and a series of side-chains. These side-chains are spoken of as receptors and are of the first or second order depending upon whether they were able to unite with one or two other cells or rather had one or two unsatisfied affinities. These side-chains were constantly being given off and had the power of uniting with toxic elements secreted by micro-organisms. Thus it was believed that the elements of nutriment going to the cells could be regarded as molecules which became a part of the cell by being joined to it through union with one of the receptors of the first order. On the other hand a toxic molecule such as that contained in the diffusible toxin of diphtheria was more complex and made up of two parts, a toxophore and a haptophore group, the haptophore group united with the receptor of the body cell and permitted the toxic effect of the toxophore group to be felt. But, as is well known, there is an antitoxin for diphtheria (discovered by Behring and Kitasato) to explain this and the antitoxin of Tetanus. Ehrlich conceives that when in excess these receptors of the second order are capable of uniting in the blood stream with the molecules of the diphtheria toxin, and of thus preventing the toxin from acting on the body

cells. The haptophore group united with a free receptor of the second order, which has been thrown off into the blood stream, and is thus anchored and holds with it the toxophore group. Ehrlich also conceives of a substance in the blood stream which he calls "complement," which is probably what we have already discussed under the name of alexin. He further speaks of "antigens," which are substances capable of producing antibodies when injected into an animal or when they develop spontaneously; and finally he uses the term amboceptor, which can be identified with what we have designated antibody or immune body, or the sensitizing substance of Bordet, unites or brings together the antigen and complement, and destruction of the antigen occurs, as we have seen when rabbit's serum is brought in contact with sheep corpuscles, where the rabbit had previously been injected with sheep corpuscles. This injection of substances into animal is spoken of as artificial, active immunization, and a rabbit treated as we have noted above is said to be immunized against sheep corpuscles and its serum is spoken of as rabbit anti-sheep serum.

One other fundamental phenomenon described by Pfeiffer in 1894, must here be mentioned. This very thorough German investigator was able to demonstrate that when cholera vibrios were injected into the peritoneal cavity of the guinea pig they underwent certain definite changes. They lost their motility, clumped, underwent granular disintegration and finally showed bacteriolysis (that is, went into solution). Since this was first demonstrated by him it has been called Pfeiffer's phenomenon. It is a very fundamental conception in immunity, as will readily be seen, and in conjunction with Bordet's fixation reaction the process stands only second to phagocytosis as a means of protection against invading hosts. Pfeiffer believed that the bactericidal

substances (as he called the substances which he believed were present in serum and brought about changes in the bacteria) were secreted by the endothelial cells. Metchnikoff and Bordet, however, were able to show that these changes were actually due to the activity of the secretion of the phagocytes, either extra or intra-cellular and did not occur in oedema fluid if blood serum was rigorously excluded.

About this time it was shown also that foreign blood serum had the power of agglutinating blood cells; for instance normal horse-serum could cause agglutination of rabbit corpuscles. Just after this it was demonstrated that certain sera caused agglutination of bacteria as well, and at first it was believed this was specific; later, however, it was shown that this was not the case and certain normal sera agglutinated bacteria indiscriminately. If, on the other hand, immune sera were used, that is, sera from animals immunized against given micro-organisms, it was found that these sera clumped the micro-organisms that had produced the immune sera. The substances were first described by Charron and Roger and were called by them "agglutinins," just as those substances bringing about agglutination of red blood corpuscles were and are called "Hæmagglutinins." Soon this agglutination was applied to various bacteria, among others, typhoid, dysentery, and *B. coli*. Widal, who applied it clinically in typhoid, has had the reaction named after him, and the Widal reaction of agglutination is now one of the ordinary clinical laboratory procedures and one of the most useful and valuable. Its often seeming unreliability is practically entirely due to lack of knowledge of its significance, and consequent inability to correctly apply it. Another very valuable diagnostic measure was learned of, about the same time, by Uhlenhuth, of Berlin, and almost simultaneously by Wassermann and Schütze. These

observers ascertained that, if an animal was injected with serum from another animal, in admixture of the serum from the second animal and that from the first a precipitate appeared in the bottom of the test tube. This is of great practical importance. Uhlenhuth was able to show, and gave us a means whereby human blood stains could be recognized as such. Rabbits are immunized against human blood, and in the presence of human blood in a suspected stain the serum from the immunized rabbit will give a precipitate. The new-formed substances in the blood have been called "Precipitins." Nuttall, who has done a great deal of very valuable work, has shown in his book on "Immunity and Blood Relationships" how it is possible to differentiate blood from different species of animals by this means. The precipitins are also found when serum from animals which have been immunized with muscle-tissue is mixed with serum from an animal of the same species, and it is possible to tell whether or not a given piece of muscle is from this species or not. The practical applicability of this in forensic medicine has recently been shown by Gay (3). Certain other substances known as cytolytic and cytotoxic bodies are found in blood serum by the injection of given organs into an animal, and on the subsequent admixture of this immune serum or cytolytic serum with the given tissue, the latter undergoes solution. Or if an animal, some of whose tissue has been injected into another animal, is taken, the serum of the second animal contains an extremely active cell poison, which becomes manifest on the injection of the serum from the immunized animal into the one whose tissue was taken. In 1903 Wright and Douglas described a substance in blood serum to which they gave the name Opsonin. It was believed to be a specific bacteriotropic substance, so that the leucocyte could more readily engulf the bacterium so acted upon. Wright later announced a method by which this opsonic activity of the blood-serum could be measured and

called it the opsonic index. It is regarded by Wright and his followers as an accurate measure of the phagocytic activity. This is doubted by many, as is shown by the work of Cole and his associates in the biological division of the clinical laboratory of the Johns Hopkins Hospital; and also by Strangways, Fitzgerald, and Whitman, working at Oxford and Cambridge.

Lastly, before considering the question of the applicability of these studies in immunity in suggesting new methods of treatment, one must pause to speak briefly of the extremely interesting condition of Anaphylaxis or hyper-susceptibility. The work up to the present has been largely experimental, but its practical application can already be seen. It is known, for instance, that when a guinea-pig is given an extremely small dose of normal horse-serum it acquires a peculiar condition of sensitivity so that after the expiration of the incubation period of two weeks (during which time the animal is acquiring the sensitivity) a second dose of normal horse-serum causes intoxication and death. The condition first described by Arthus, and Roscman and Anderson, (4), of Washington, has been most carefully studied by Gay and Southard (5), of Boston, whose work on the subject stands out as a masterly contribution to our present-day knowledge of Anaphylaxis.

Such a consideration of some of the more interesting and more easily understood phenomena of immunity can be best brought to a close by pausing for a moment to consider the advances in treatment that have resulted.

We have seen how an animal may be immunized by the inoculation of bacteria, red blood cells, etc., so that its sera, acting in conjunction with alexin is able after a period of inoculation, during which time the animal is becoming immunized) to destroy the substance originally injected. This condition is called active artificial immunity, because the vital processes of the

body enter into its production. A second form of immunity, known as passive immunity, is brought about by the introduction of the virus of the organism in an attenuated form, the organism itself in an attenuated form, or by the transfer of an immune serum from an animal or individual in whom an active artificial immunity has been produced.

Jenner was the first to introduce vaccination against smallpox by the introduction of an attenuated virus, that of cow pox. Later Pasteur introduced his treatment for hydrophobia or rabies by vaccination, with the cord of rabies inoculated with "*virus fixe*," attenuated by being allowed to stand, and undergoing dessication. This work of Pasteur is alone sufficient to forever justify rational, intelligent and necessary animal experimentation. By the introduction of the Pasteur treatment, a condition which is invariably fatal when fully developed, has been successfully combated so that now mortality from the disease is less than one per cent., although the number of undoubted cases is very great. In the Boston City Hospital within the past six months two cases of hydrophobia have been admitted, both terminating fatally.

The antitoxin for diphtheria has greatly reduced the mortality from that disease and tetanus antitoxin is also claimed to be of value by many. The anti-meningitic serum of Flexner and Jobling and of Wassermann is apparently of extreme value in cerebro-spinal meningitis, although its efficacy will be more easily given its correct valuation when a severe epidemic arises and the serum is extensively used. Other sera such as anti-pneumococcic—Marmorek's for tuberculosis, and that of Chantemesse for typhoid, have not been sufficiently tried out as yet, although their respective discoverers vouch for their efficacy.

Besides the vaccines for smallpox and rabies, many bacterial vaccines have been lately introduced—Wright's for typhoid, which apparently is of consider-

able value, especially in war-times. Also the gonococcus vaccine, useful in late cases of arthritis appearing as sequelæ of specific arthritis, but due to the same cause. Staphylococcus vaccine and tubercle vaccine in local conditions are also useful. All these vaccines are prepared from fresh cultures of the organism destroyed by heat or by a twenty-five per cent. galactose solution or has been shown recently by Weaver and Harris (6) to be more useful. An estimated number of these organisms suspended in normal saline is given subcutaneously. Certain cases of streptococcic and other septicæmias have occasionally responded to such treatment in a marvellous fashion and the bacterial vaccines seem to have a very likely future in the treatment of such conditions as have been indicated.

Immunity to-day opens broader fields of research than any other in the realms of scientific medicine, and while hygienic and preventive measures are ever to be striven for as the ideals to which we hope eventually to attain, meanwhile the strengthening of the powers of resistance of the vital forces of the organism is something which can be gone on with now, and the weapons at hand are wonderfully potent. The mechanism of many, as yet undiscovered, await the revealing hand of the worker in immunity.

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THE CEREBRO-SPINAL FLUID IN RELATION TO
THE DIAGNOSIS OF METASYPHILIS OF THE
NERVOUS SYSTEM.

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In the brief review here offered of this important question I shall confine myself entirely to those features which experience has shewn to be most useful and applicable in relation to diagnosis. At the outset it may be stated that the evidence as to the value of the examination of the cerebro-spinal fluid is now so complete that it is unjustifiable to express an opinion in regard to any doubtful case of metasyphilis (tabes and general paralysis) before this examination has been carried out.

I shall not consider the technique of the examination, which has of late years become so simple. An excellent account of this will be found in Purves Stewart's writings, and I may refer to a publication of my own in which a short and accurate method of counting the cells is described whereby no apparatus is needed other than a microscope, a needle and test tube, and the ordinary hæmocytometer.

The features of the cerebro-spinal fluid have been thoroughly studied from a great many aspects but several of these, such as the osmotic tension, electrical conductivity, permeability, toxicity, etc., will not be mentioned here inasmuch as, though interesting from other points of view, they have not as yet been shewn to

possess such value in practical diagnosis as to render themselves in any way a necessary part of routine examination.

It would also be quite impracticable here to detail the actual work that has been done or even the number of cases and results obtained by each individual author, as for that purpose a volume would be necessary. The bibliography given may to some extent supplement both these deficiencies for those readers desirous of pursuing the subject in greater detail, as several thousand cases are referred to in the articles there mentioned. I shall thus restrict myself to a statement of the conclusions that those researches seem definitely to warrant. The subject may be divided into four sections.

(A) *Physical Properties.*

Of the many matters studied in this connection the one practical piece of knowledge that seems to issue is that the pressure of the fluid is raised in most cases of metasymphilis; this fact was emphasized first in 1901 by Schäfer, and stress has since been laid on it, particularly by Decoubaix, Fuchs, Henkel, Pegna, Rosenthal and Skocznski. The rise is decidedly greater in the case of general paralysis, in which the pressure is commonly twice and may reach six times that of the normal.

Facts less important in diagnosis are the lowering of the freezing-point and the rise in specific gravity, both also more prominent in general paralysis than in tabes.

(B) *Chemical Properties.*

The most important and also most easily ascertainable fact here is the relatively large quantity of albumen. Whereas, normally, no albumen or only a minimal trace is found, the only proteid present being a slight amount of globulin, in metasymphilis nucleo-proteid, albumen and globulin are found in considerable quantity. The presence

of the first named is especially significant as indicating with certainty the presence of organic changes. The total amount of proteid may reach three grammes per litre. The increase in globulin is greater, and of more significance, than that in albumin. The increase is greater with general paralysis than with tabes, and much greater with metasyphilis than with tertiary syphilis of the nervous system. It is especially great at the onset of the disease and during the exacerbations. Though the proteid is probably derived from leucolysis, as Feuille pointed out, the amount of it is by no means always proportional to the number of cells present in the liquid and is often great in the later stages when the number of cells may have considerably diminished. First observed by Achard, Loeper and Lanbry in 1901, the importance of this sign in diagnosis has of late been greatly emphasized by Coriat, Decoubaix, Guillain, Henkel, Marie, Parant, Pegna, Schaefer, Viollet, Zilanakis and others.

An observation less easily made, and of which the interpretation is also less certain, is the presence of a considerable quantity of choline, found especially in cases of general paralysis. The original technique employed by Mott and Halliburton has of late been much criticised by Allan, Cramer, French, Rieländer, Mansfield, Rosenheim, Kauffman, Skocznski and Vincent, and subsequently modified. Their conclusions have, however, been on the whole confirmed by Coriat, Donath, Rosenfeld, Wilson and others.

It has further been stated that lactic acid and dextrose may be found in some quantity in general paralysis.

(C) *Cytology.*

Unquestionably one of the most important discoveries in neurology made during the past few years has been the demonstration of the fact that lymphocytosis of the cerebro-spinal fluid is almost constantly present in meta-

syphilis of the nervous system. This discovery, made in 1900 by Ravault, Sicard and Widal, was soon generally recognised, in spite of early efforts made to deprecate its value by Armand-Delille and Camus, Nieder and Mamlock and others.*

Several different varieties of cells may be found in cases of metasyphilis, the chief being mononuclear lymphocytes, plasma cells, and polymorpho-nuclear leucocytes. There are never very many of the last named except during the paroxysmal seizures of general paralysis; the lymphocytes are always the most numerous.

With regard to the different lesions present the following statements may be made. Lymphocytosis may occur at any stage of syphilis, apart from implication of the nervous system, but in such case is always minimal in amount; any considerable lymphocytosis in a case of syphilis should always arouse suspicion of implication of the nervous system. Further, the lymphocytosis in cases of syphilitic disease of the nervous system is slight and never reaches the proportions found in case of metasyphilis. It is considerably greater in cases of general paralysis than in cases of tabes, and in the former affection many hundreds may be found to a cubic millimeter. The pathological significance of the sign is not yet decided. The old French view that it was synonymous with meningeal irritation has been much controverted

*The importance of the observation has since been very widely confirmed—in France by Achard, Ballet, Babinski, Bèlètre, Boidin, Brissaud, Bruandet, Chauffard, Castin, Crouzon, Darré, Delheru, Demanche, Duflos, Dupré, Froin, Gombault, Grenet, Halbron, Jaulin, Joffroy, Marie, Mercier, Minot, Milian, Monod, Ninot, Pichenot, Ravaut, Roux, Sicard, Souques, Vaquez, Wilson; in Germany and Switzerland by Abraham, Donath, Erb, Fankhausen, E. S. Fraenkel, Fischer, Fuchs, Gerhardt, Henkel, Liebscher, Merzbacher, Meyer, Nissl, Orgelmeister, Rehm, Rosenthal, Schäfer, Schlsinger, Siemerling, Schönborn, Skoczynski, Ziegenhagen; in America by Cramer, Cornell, Coriat, Dana, Farrar, J. Fraenkel, Pasrayan; in England by Edwin Bramwell, Macfie Campbell, Mott, Purves Stewart; in Italy by Catòla, Pegna, Pighini, Severino; in Belgium by De Buck and Decoubaix, in Greece by Zilanakis, in Holland by Van der Kolk, in Hungary by Balogh, and in Roumania by Marinesco and Minea.

of late by several German writers, and it may now be considered as disproved. Fischer has attempted to correlate the sign with cellular infiltration of the lumbar meninges, but this has been opposed by Alzheimer and others, and is certainly far from being demonstrated. The present view is that marked lymphocytosis is to be correlated with the metasyphilitic affection rather than with the causative syphilis. Lymphocytosis occurs in cases of juvenile ("inherited") metasyphilis as well as in adult cases, though in the former it is, according to Van der Kolk, less in extent. Bramwell has described an interesting case of juvenile general paralysis which showed marked lymphocytosis, although no history of syphilis could be obtained, an occurrence common amongst adults.

The value of the sign is, therefore, of the highest importance in the diagnosis of metasyphilis. It is perhaps the most constant physical sign of this affection. Henkel, for instance, found it present in *every one* of 85 cases of general paralysis examined, and the constant presence of it in even a large series is by no means unusual.

The extent and constancy of the lymphocytosis varies with the stage of the disease. It is commonest and greatest at the onset, a fact of especial significance for diagnostic purposes. In the same case, if repeatedly examined, it is commonly found that the lymphocytosis diminishes towards the end of the disease. Exceptionally on the other hand, as in a case published by Achard and Demanche, it may develop only late.. It is most marked in cases running an acute course, and during paroxysmal exacerbations. It thus is greater during the seizures in general paralysis and also during the curious febrile disturbances accompanied by an increase in the polymorphonuclear cells in both the blood and cerebrospinal fluid, that occur in this affection.

As stated above, the lymphocytosis cannot be closely correlated with the excess of albumen, and, as the former is more marked early in the case and the latter late, it is clear that both signs should always be examined for. Particularly is this so because, as Liebscher has shewn, an excess of albumen is rare in lues of the nervous system, so that lymphocytosis plus an excess of albumen speaks more in favour of metasyphilis as opposed to nervous lues than does lymphocytosis alone. As Wilson has shewn, there is further no distinct correlation between lymphocytosis and the amount of choline present.

(D) *Serodiagnosis*.*

The honour of the above discoveries belongs almost exclusively to the French school, but German observers have lately responded by introducing a brilliant method of research in the present connection that promises to have most important consequences, both clinically and pathologically. With this new method the names of Wassermann and Plaut are intimately associated.

The original cause of metasyphilitic diseases in question, Schaudinn's Spirochæte, has never been found in the cerebro-spinal fluid in these cases, as indeed might have been expected. Catola has carefully examined, with this aim, five cases of general paralysis, post-mortem, and Marinesco and Minea fifteen cases of tabes during life with negative results.

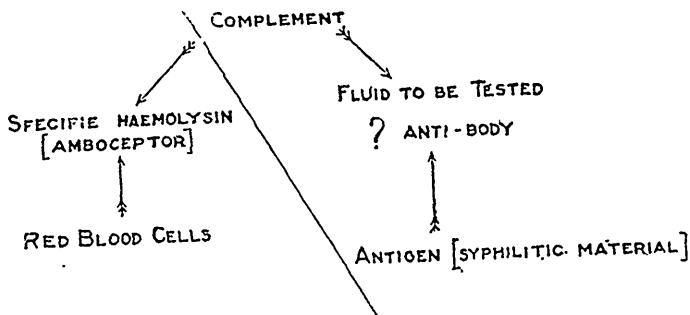
That, however, the direct effects of this organism on the central nervous system can be demonstrated has been proved within the last couple of years. Before describing the clinical aspect of the question a few words are perhaps desirable on some elementary points concerning the extensions of the Bordet reaction. It was

* A full account of this subject will be found in an article by the present writer, entitled "A Review of our Present Knowledge concerning the Sero-diagnosis of General Paralysis," in the April number of the American Journal of Insanity, 1909.

shown by Bordet eight years ago that when cytolysis takes place, two substances are necessary for the solution of the antigen (animal cell or bacterium as the case may be). These are (1) a non-specific substance, or complement, found in all blood sera, and capable of being destroyed by being heated to 56° C., and (2) a specific substance, or amboceptor, found only in the sera of such individuals that have been previously injected with the corresponding antigen—the amboceptor being thus evoked as a response to the foreign body—and not destroyed at 56° C. It follows that if two of these three bodies are present in a fluid and cytolysis does not take place, the third one must be absent; thus if the antigen is not dissolved on being added to its corresponding amboceptor, the complement must be missing. In this way we can test for the presence or absence of complement.

Returning now to the question of metasyphilis. If an extract of a syphilitic organ—for instance, the liver of a syphilitic foetus in which the presence of spirochaetes has been demonstrated—*i.e.*, an antigen-containing solution, is added to a serum containing both complement and the corresponding amboceptor, or syphilitic antibody, then cytolysis occurs and the three substances are bound together. If on the other hand, in spite of the known presence of the antigen and complement, no cytolysis occurs, then the serum tested could not have contained any syphilitic anti-body. Whether cytolysis has or has not taken place is shewn in the following indirect way. If to the mixture just described is added (1) the red blood cells of an animal, together with (2) the blood serum from another animal which has previously been injected with the red cells of the first animal and which, therefore, contains the corresponding amboceptor, then hæmolysis or laking, which can easily be seen, may or may not take place. If it does not take place we must assume that it is due to the fact that the original mix-

ture contained no free complement, and, therefore, that the original complement must have been combined with the syphilitic antigen, a combination only possible if the serum being tested contained a syphilitic anti-body or amboceptor. If hæmolysis does take place, then free complement must have been present; *i. e.*, in the original mixture combination of complement with antigen did not occur because no anti-body was present. Thus hæmolysis indicates the absence of syphilitic anti-bodies in the serum being tested, and failure of hæmolysis indicates the presence of such anti-bodies. The accompanying diagram will perhaps make this point clearer. In



other words the test turns on the determination whether or not free complement remains after the mixture of the serum that is being tested and known syphilitic material. Care must of course be taken that no complement is present in the second or animal serum added and this is ensured by first heating it. Further, no test should ever be carried out without a simultaneous control experiment with serum from a non-syphilitic individual being performed.

In 1906 Wassermann, Neisser and Bruck demonstrated by this method that specific syphilitic anti-bodies were present in the blood serum of a certain percentage of syphilitic patients. Neisser, Bruck and Schucht tested the blood of 261 such patients and found anti-bodies in the blood of 27% of the cases showing active secondary manifestations, and in only 11% of tertiary cases. On the other hand syphilitic anti-bodies are *almost constantly* present in the blood serum of patients with metasyphilis. Thus in Wassermann and Plaut's original investigations anti-bodies were found in the serum of 19 out of 20 cases of general paralysis and Plaut in his later investigations found them in every one out of 180 cases; the same holds good for tabes. This contrast between 11 per cent of tertiary syphilis and 100 per cent. of metasyphilis is most striking.

In the same year Wassermann and Plaut examined the cerebro-spinal fluid of 54 cases of general paralysis in Berlin and found the test positive in 41 cases, doubtful in 8, and negative in 5. Marie and Levaditi found it positive in 29 out of 39 cases, some of the negative cases being, however, of uncertain diagnosis. Plaut, in 1907, reported 44 cases from Munich, in which the findings were positive in 41 cases, doubtful in 2 and negative in 1. These results have been confirmed by later writers, and altogether some thousands of cases have now been examined. On the other hand most authors have found the cerebro-spinal fluid free from anti-bodies in all cases of tertiary lues cerebri that they have examined.

The value of the test may thus be summarised. The presence of syphilitic anti-bodies in the blood serum is certain evidence of past syphilis, and, in any chronic disease of the nervous system, speaks decidedly in favour of the presence of metasyphilis. The presence of them in the cerebro-spinal fluid is almost pathognomonic of metasyphilis, is an extremely frequent sign, and is therefore one of the most valuable evidences of meta-

syphilis that we possess. Even in the cases of metasymphilis in which they are not found in the cerebro-spinal fluid they may be found in the blood serum, thus demonstrating the syphilitic nature of the condition.

Marie and Levaditi have concluded, chiefly from repeated examinations of the same cases, that antibodies are more constantly present in the late than in the early stages and that they bear a relation to the extent and intensity of the affection. Plaut has objected to this that the variation is probably due to the varying intensity of reaction that the same fluid, and hence also different fluids, give towards different examples of syphilitic material. In over 100 cases he finds no correlation between the intensity of the reaction and the stage or severity of the disease. The reaction appears to be also independent of the interval between the disease and the syphilitic infection, of the extent of anti-syphilitic treatment, and of the degree of lymphocytosis and albumen increase. Most interesting is the fact that there is no correlation between the reaction and the history of syphilis; Morgenroth and Stertz, for instance, obtained a positive history in only one out of eight cases in which anti-bodies were demonstrable.

In July, 1907, Fornet and Schereschewsky published the results of some precipitation tests in which they found that the serum of metasymphilitic patients caused a precipitate when added to the serum of a known case of syphilis. So far, criticism by Alzheimer, Plaut and others, has shewn that this method though more easily applicable than the one described above is not so reliable.

(E) *Summary.*

The evidence available goes to shew that examination of the cerebro-spinal fluid is the most precious means at our disposal for the diagnosis of metasymphilitic affections and should never be omitted in any doubtful

case. The serological test is probably the most valuable step in this examination, but is inconvenient of application, and is in fact impossible, except where a laboratory for vivisection is accessible.

The three most important points ascertainable by simple examination of the cerebro-spinal fluid are: increased pressure, excess of albumen, lymphocytosis. This triad is practically diagnostic of general paralysis in any case of mental disorder, and of tabes in any chronic disease of the nervous system where no menal disturbance is present.

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FEEBLE-MINDEDNESS IN CHILDREN.

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It is truly surprising that people so slowly see the folly of waiting till the feeble-minded child grows up to be an unemployable, a drunkard, a jail-bird, or a prostitute before lifting a finger to care properly for those who can never care properly for themselves, or to protect the community by preventing the waste, the inefficiency, the disgrace caused by our present policy of neglect. Not long since an able administrator, a Government official, whose personal efficiency and kindness of heart are beyond question, said, in reply to my plea that the most effective work for the feeble-minded must begin with feeble-minded children: "Would you let the grown-up people that do all the harm go, and spend your time on the children?"

He forgot for the moment how quickly the child of 7 years in 1899 becomes the young adult of 17 years in 1909. The year 1899 seems like yesterday, but we have now in the Police Court of Toronto a case in which two feeble-minded girls, both under 17, have done deeds of wickedness and immorality (at the temptation of two full-grown men *not feeble-minded*) fit for Sodom and Gomorrah. They were both recognized as feeble-minded when they were at school, and we should have realized then their need of care and have given it. He forgot, too, the untold saving in character, in future prospects, secured by care of such feeble-minded children. These two girls now are probably ruined for life. The cells in the Mercer are largely filled by just such. More than one hundred such persons are continually in and out of the Toronto Police Court. Think of the waste of money involved in the operation of our present antiquated and unscientific methods of dealing with such "criminals." A great deal of it might be saved. They are not really responsible, and should never

have had the chance to become criminals. The waste of money is bad enough, but it dwindles into insignificance when we think of the lowering of the moral tone of the community caused by one such feeble-minded woman, unprotected. I have letters in my possession entreating the Government to take action in certain well-known cases, where the writer says that the abode of this feeble-minded woman is a "plague-spot" in an otherwise respectable neighborhood. Why allow the poor thing to become such a temptation and source of evil? Why not take charge of her as soon as the condition is recognized, that is, at school? In investigating the two cases referred to above, I found that one girl had attended a country school, and I asked the mother if the girl had got on well at school. "Oh, no, she didn't," answered the mother, readily enough. "She did not get on well at all, and that was why I kept her at school so much longer than the others." This girl left school at 14 years of age and had got about as far as the Second book. The reply of the mother is significant, when we remember that usually the very last thing people will admit is that there is anything wrong with their children mentally.

The other girl had attended two of the best public schools in Toronto. I applied to her teachers for information and received at once the same unhesitating answer. It had been practically impossible to teach her. She could read and write a little and that was all. The mental defect was marked. And these two unfortunates were exposed to the fierce temptations and passions of life. In these cases of the feeble-minded, the body and the bodily appetites are fully developed. The powers of mind, judgment, reason, self-control are undeveloped. They never develop, but remain at the level of such powers in a child of about nine years old. We know how we feel when we come across the case of a child of such tender years being by some means the victim of such wickedness.

Dr. A. F. Tredgold, Medical Expert to the Royal Commission on the Feeble-Minded, in his recent valuable work (*Mental Deficiency*. London: Baillière, Tindall & Cox), makes a convenient classification of all feeble-minded children into three grades. The first grade is composed of children who can do some elementary school work. They can write a simple letter, can read children's books, can do the first four rules of arithmetic, can do a little mental arithmetic. They can often do messages and have some knowledge of money. They can do handiwork well, sometimes even beautifully. They have some common sense, but lack resource, judgment and initiative.

The second grade fall considerably below the first in school work, and in handiwork also, but not as much as in school work. They are decidedly inferior in arithmetic, and can only read and write small and simple words, or not at all. They can do manual work, but not as well, and require more constant supervision and help and direction.

The third grade are not very much above the imbeciles. At a special school they learn some manual work and good habits, becoming tidy, regular and obedient, and almost always happy. They can hardly do any school work at all.

Certain well-known educational principles may be applied with great success to the care, training and education of feeble-minded children. The first is the law of self-activity. Just as the salvation of the physically defective is found in letting them take up everything they are equal to, or can be made equal to, so it is with the mentally defective. We can learn a good deal about the education of the mentally defective by studying what has already been proved in the education of the physically defective. First of all is the fact that they need a chance to work. So do the feeble-minded. And they can do a great deal of work. They can profit

by training and instruction. They are capable of useful work. It would be almost impossible to mention any business or trade at which they could not do something, if under skilled and efficient supervision. Another principle is that of adjusting the task to the pupil's powers. Here is one who can not lace his own shoes. Give him a model—a simpler shoe, with bigger holes, and with joy of effort and delight he masters this, to him, great task. Another can fit two clothes pins together and will practise this for hours. Another cannot close his hand well, and he begins to make a rope, and by the time he has accomplished this new task, he can use the fingers of both hands with an accuracy and skill he never could before.

Another principle is that in order to make progress, to be educated, we must feel that we count. I wonder if some of us normal people were transported to another planet, and found ourselves hopelessly outclassed, how long we could stand it? Hopelessly outclassed. EVERYBODY better, wiser, stronger, abler, more lovable and more loved than we. Terrible fate—the terrible fate of the feeble-minded. But class them with their equals and at once their self-respect comes up. They find themselves of some account. They are trusted. They are leaders in some little way. They are not outclassed. They are with their peers. One of the worst cases of feeble-mindedness in this Province, a woman of 28 who had had four children illustrates this. Her mother and all her brothers and sisters are feeble-minded. Three generations and twelve persons, all feeble-minded in this one group. This woman was placed in a Charitable Institution and did only fairly. But one day I was driven to beg admittance among these women for a feeble-minded girl of 12 years. I had nowhere else in the world to take her. And this poor mother, who should never have been a mother, who had forgotten her

own children, saw the new inmate, yet more helpless than herself. She pounced upon her, arranged her clothing, insisted on administering a bath, and proudly announced to the audience of inmates that as long as she was there she would see "that there kid behaved herself and kept herself clean." And she has kept her word.

It must be admitted that the powers of work of the feeble-minded are considerable. They can do almost anything in this way that a normal person can do, but someone must supply the brain power. What they cannot do is to manage their own affairs. What they lack is prudence, self-control, will-power, judgment, restraint—they cannot take care of themselves. For them book learning is very largely thrown away. A good many can be taught to read and write, and perhaps to count a little. That is all. An hour a day seems to be the limit for "book learning."

All they learn should be of use to them in after life. They *can* do what they are told. They can imitate, so we should teach them habits of imitation which will do instead of habits of reason.

They may and often do become self-supporting, or nearly so, but never self-controlling. At Starcross, near Exeter, in England, I have seen them working with ease and comfort at about twenty different trades, making beautiful Honiton lace, weaving cloth, or executing orders for wood-carving which brought in much money besides giving all the benefit of the work. They need most skilful care; physical defects are twice as common in feeble-minded children as in normal children.

The first class for the feeble-minded was opened in Halle, Prussian Saxony, by the principal, Herr Haupt, September 28, 1859. England, the United States, France, Finland, Norway, Denmark, Sweden, Switzerland, have since established special classes. There are at present in Germany 203 special schools with 13,100 pupils. England began in 1892, the United States in

1894. In New York there are now 41 special classes with 731 pupils. I have had the privilege of visiting some of these classes, and it is an inspiration to think of the work that goes on there under Miss Farrell and Dr. Thompson. Philadelphia has ten special classes and one special school for the feeble-minded. Boston and Chicago are also doing a good work for mentally defective children, and other places are following fast.

Estimates of the proportion of the feeble-minded to the general school population under fourteen vary from 1 per cent. to one-tenth of 1 per cent. In Ontario it is estimated at about .3 to .5 per 1,000.

No human being is a negligible quantity and we have made a great mistake in the past in thinking that the school could neglect the feeble-minded child. No feeble-minded child is a person you can neglect. You could almost protect the next generation from the problem of the feeble-minded if the school and the state did their duty. The feeble-minded can and ought to be educated to be useful to themselves and not harmful to others. The special class should be a clearing-house where the 66 per cent. or more of special scholars who will always be dependent and need lifelong care may be recognized, carefully studied, and placed in home schools or parental schools which will be their permanent home. This is their "firing-line." This is the only way of dealing with the problem.

The rights of feeble-minded children are now recognized by law in Great Britain.

In the Defective and Epileptic Children (Education) Act, 62 and 63 Victoria, Chapter 32, 1899, we find feeble-minded children defined as those who, "not being imbecile and not being merely dull and backward, are defective—that is to say, by reason of mental defect, are incapable of receiving proper benefit from the instruction in the ordinary public elementary schools, but are not incapable by reason of such defect of receiving

benefit from instruction in such special classes and schools as are in this Act mentioned."

Another useful definition and one accepted by the Royal Commission on the Care and Control of the Feeble-minded, (appointed by His Majesty in 1904,) whose Report, issued in 1908, is the chief event of interest recently to those who are devoting themselves to the study of this question is as follows: "A feeble-minded person is one who is capable of earning a living under favourable circumstances, but is incapable, from mental defect existing from birth or from an early age, (a) of competing on equal terms with his normal fellows, or (b) of managing himself and his affairs with ordinary prudence."

The signs that the time is coming when the Government and the people of Ontario will take care for the feeble-minded are welcome. Nothing can be more truly philanthropic or statesmanlike than to care for the poor and needy, and the feeble-minded, especially feeble-minded children, are the poorest and most needy of all.

IMMIGRATION OF DEFECTIVES.

During the last year a great deal of criticism has been offered regarding the facts and figures set forth in last year's Annual Report, and also in the July, 1908, Bulletin, in respect to the number of defectives being brought to us from the Old World. It has been suggested that we have magnified the evil and have been unfair in drawing conclusions from the data at hand. Unfortunately the gravity of the situation has not been magnified, and it is not going too far to say that we, of all others, are in the best position to appreciate the dangers to be expected from the importation of mental defectives. The bare facts are suggestive enough; an analysis of them makes us marvel at the complacency of those who calmly accuse us of a want of patriotism in decrying certain kinds of immigration from the old country. No matter how figures may be twisted by the pseudo-patriotic enthusiast, when building up beautiful philanthropic plans which are to enable the slum weakling to shake off the stigmata of degeneracy, in the free air of the prairies, or in the forests of the north, yet facts based on experience must prove in the end a far safer guide than finely spun theories, which are founded on sentiment rather than common sense. As has been pointed out before—and this cannot be too often repeated—much of the success of a nation will depend on the quality of the stock from which it springs, and any one who has time to investigate the results of the early immigration to Canada, will learn something of interest concerning the possibilities and probabilities of the new immigration. Investigation into the antecedents of certain early settlers will show that it would have been wise to scan closely the possibilities even in the days when settlers were far more essential to the success of Canada than now. A recent writer who was active in

imposing on Canada one of the biggest burdens in the way of alien population that we have to carry, says "Canadians, with a patriotic selfishness that is not admirable, often ask why they should have the uplifting of inferior races? Why should not Europe cure the people Europe has spoilt? Is it not rather wiser for a nation to share in the task of uplifting humanity rather than to try and maintain an exclusive virtue, limited by a political boundary and safeguarded by deliberate selfishness?" This kind of sophistry has been employed even by some of our Canadian writers, but while it may be comforting to those who have pangs of conscience regarding a manifest injury they have done to our nation, yet does not help us in our time of trial. We must never forget the manifest truth of the old writer who said :

"For they have sown the wind, and they shall reap the whirlwind."

A brief perusal of the criminal annals for the last year or two will give some idea of the harvest we are already beginning to gather. Murders committed by epileptics shipped out as "nuisances;" several murders by low types of foreigners; a wife-beating tragedy unique in our history, and so the story goes. Do not the figures on gaol population, furnished by Inspector Armstrong last year, speak for themselves? But without dealing in generalities, let us see how things have been with us in the Toronto Hospital for the Insane in the last twelve months, a period during which immigration has fallen off and inspection is said to have been far more rigid than formerly. Of two hundred and fifty-eight patients admitted to this Institution no less than one hundred and sixteen were foreign born: that is 44½ per cent. If that proportion had been 18 per cent. or 20 per cent. it would have been normal, but the startling fact is in connection with the nationality of admissions; no less than 65 of these being English, 13 Irish

and 10 Scotch; 15 came from the United States; the immigration from that country now being an important factor in the increase of population. Other countries account for thirteen, thus showing that the immigration requiring the most careful scrutiny is that from the British Isles, especially that coming from the cities, in the slums of which degeneracy and crime find a suitable soil for development. Forty-six of the admissions had been resident but a brief period, and no less than thirty patients were deported during the twelve months. If the Deportation Act had been a little broader in its provisions and made the residence rule extend to three years, the number to be deported would have been larger. We would suggest a residence rule of four years as advisable, as this would enable us to weed out defectives pretty thoroughly, as well as discover those whose former history cannot be learned at the time of landing.

It is a common experience to find that a patient admitted has had an asylum residence in the old land and has emigrated to get away from the history of this thing. One has deep sympathy for the sufferers, but after all should sentiment sway us when dealing with a subject that means the very life of a nation?

An analysis of the admissions proves most strikingly the importance of carefully scrutinizing those who come to our shores.

How some of them can pass any thorough system of inspection is a mystery, the general paretic, the precocious dement, the obvious degenerate all slip by and reach us in a surprisingly short time. Surely it would be wisdom and good economy on the part of the Federal authorities to have some of their medical inspectors trained in psychiatry; even a mere tyro in the study of psychiatric problems would be able to detect the weak spots in many of those who at present safely run the gauntlet of port of arrival inspection.

The importation of boys and girls of distinctly defective type should be absolutely discouraged. Our experiences with these weaklings make us realize how great a menace they are, and how careful we should be to make a thorough examination of their antecedents before admitting them. Better still would be to exclude them altogether, and when I say this I voice the opinion of many of those who have had to deal with these questions practically.

The following press despatch from England shows that the Old Country authorities are beginning to wake up to the fact that we are capable of thinking and acting for ourselves. I do not agree though, with the conclusions of the magistrate in regard to the valuable experience the boys would receive. If they are of the type we suppose them to be, it is simply cruelty to expose them to unnecessary strain and hardship.

DEPORTING EMIGRANTS.

British Magistrate thinks it not to credit of Canada.

(Canadian Associated Press Despatch.)

London, Feby. 5th.—Before signing a declaration necessary in connection with the emigration of eight boys to Canada from Old Street, Magistrate Biron said he did not doubt it would be a good experience for the boys, but there was no guarantee that they would not soon be sent back here. He referred to the Oshawa deportation case, and said such a proceeding was not good for prospective emigrants or the credit of Canada.
