INTERNATIONAL CONFERENCE OF THE
MEDICAL PRESS.

At the International Medical Congress held in Rome in 1894, a meeting of medical journalists representing various countries was held, at which the opinion was generally expressed that it would be useful to form an international committee. Nothing definite, however, was done until July, 1900, when the First International Congress of the Medical Press was held in Paris. Numerous papers were read at this Congress, and prolonged discussions took place which were subsequently published in a volume, but the Congress failed to arrive at any definite decisions.

At the suggestion of Dr. Blondel of Paris it was determined that before another Congress was held a meeting should take place of delegates of various countries, in order to draw up rules and regulations for an International Association. This meeting took place on April 7th, 8th, and 9th, at Monaco, at the invitation of the Société Médicale de Monaco, under the honorary presidency of His Serene Highness the Prince of Monaco. The Prince, who, as is well known, is an enthusiastic student of marine phenomena, is building a magnificent Maritime Museum on the hill of Monaco, where already certain laboratories are installed; eventually this will become without doubt one of the most important of the maritime stations for the study of marine organisms.

The first meeting was held on the afternoon of April 7th, in one of the large halls of this museum; the chair was taken by Professor Cornil, of Paris, and the Prince of Monaco was present. The countries represented were Austria, Belgium, Bohemia, Denmark, England, France, the German Empire, Holland, Italy, and Norway. The proceedings were opened by the Governor-General of Monaco, who delivered an address of welcome. He was followed by Dr. Godineau, President of the Société Médicale de Monaco. Professor Cornil then thanked the Prince for the interest which he had shown in the subject and for his hospitality to the delegates. Dr. Blondel, the Secretary-General, indicated the scope of the work before the meeting, and delegates representing each country then expressed the thanks of the several nations to the Society and to the Prince. Subsequently a visit was paid under the guidance of the Prince to the various parts of the museum which are already completed. The delegates were received by the Prince at the Palace on the same evening.

Four prolonged meetings for the transaction of business were held on the two following days, and the proposals put forward on behalf of France, Germany, and England were thoroughly discussed, every disposition being shown by all the delegates present to arrive at useful conclusions, and to this end to make mutual concessions. The utmost cordiality prevailed, and the good relations established will, there is every reason to hope, bear good fruit in the future. That this was so is largely due to the courtesy and impartiality displayed by the Chairman. Professor Cornil, and to the energy and organizing ability of Dr. Blondel. On the proposition of the Spanish representatives, it was resolved to hold a meeting at the time of the International Medical Congress which is to assemble at Madrid in 1903.

At the concluding meeting the Prince was again present, and invited the delegates to attend the opening of a new hospital for Monaco which has been erected at his cost upon the slopes of the Tête de Chien which rises behind the town of Monaco. This hospital is built on the pavilion system in one story, and is in every respect complete, every regard being given to modern opinions concerning the necessity for aseptic precautions. Each large ward will contain 12 beds. There are also numerous isolation rooms, and a special department for surgery, with an excellent operating room. There is a maternity department with a lying-in room and separate small wards, and a pavilion for paying patients. The hospital altogether will accommodate about 100 patients, and is provided with disinfecting appliances, *post-mortem* rooms, laundry, and mortuary, as well as with a chapel. The nursing will be carried out by a sisterhood.

In the evening a dinner was given by the Société Médicale de Monaco, at which the Prince presided, and speeches were made by the Prince, Professor Charles Richet of Paris, and others representing the various nationalities. On April 10th

a visit was paid to the Observatory of Nice, and on the same evening a large party, including not only the delegates, but also representatives of the medical profession from most of the towns on the Riviera, were entertained at a banquet by the municipality of Nice under the presidency of the Mayor.

For the admirable arrangements made for the business of the Conference and the comfort of the delegates the best thanks are due to the Société Médicale de Monaco, and to its courteous and energetic secretary Dr. Guimbail. We venture to add that the medical profession generally is indebted to the Prince of Monaco for the interest which he has displayed in a department of medical work that seldom receives much attention from rulers or governors. The Prince has published an admirably illustrated series of reports on the scientific results of his investigations into the flora of the sea, directed by men of science who are afforded every opportunity for prosecuting their studies in the Prince's yacht, the Princess Alice, which is specially fitted with laboratories for the study and immediate preservation of marine organisms. The delegates had the opportunity of visiting this yacht, over which they were conducted by Captain Carr, R.N.R., her commander.

A SUMMARY AND ANALYSIS OF RECENT
OBSERVATIONS AND THEORIES

AS TO THE

PROCESSES OF INFECTION AND PROTECTION
IN THE ORGANISM.

By H. W. ARMIT, M.R.C.S.Eng., L.R.C.P.Lond.,

(Concluded from page 920).

IV.—CRITICISM AND ADAPTATION OF SIDE-CHAIN THEORY.
Objections and Criticisms of Ehrlich's Views.

VARIOUS observers have taken exception to parts of the teaching of Ehrlich. Bordet (*loc. cit.*) denies the specificity of the immune body. He calls it *substance sensibilisatrice*, and ascribes to it the function of rendering the red cell capable of being directly attacked by the poison, and regards it as incapable of exercising any specific chemical affinity. Buchner¹ has given his support to Bordet's views, and is largely responsible for their development. According to these two investigators, the activity of a haemolysin depends on the presence of alexin. They presuppose that a normal serum contains a protective body, which acts in destroying any foreign cell (blood cell, bacterium, and the like), and has the character of a protolytic enzyme. This body is alexin. It is destroyed (functionally) by heating to 55° C. Each species contains but one alexin, and each alexin is peculiar to the species in which it exists. Bordet² performed the following experiment. (Ehrlich and Bordet have each repeated the other's experiments, and only differ in their interpretations.) Two equal mixtures were prepared, each containing 0.2 c.cm. of the serum of a guinea-pig previously treated with rabbit's blood, and 1.0 c.cm. of rabbit's serum previously treated with hen's blood rendered inactive by being heated to 56° C. Each mixture would contain two *substances sensibilisatrices* and one alexin. To one part was added rabbit's blood cells first, and then hen's blood cells; to the other the hen's blood cells were added before the rabbit's. Only the red cells, which were first added, were dissolved in each case. This, he argued, was contrary to what would have taken place were Ehrlich's theory correct. In this experiment, however, each mixture would contain a specific amboceptor, which would attach itself to the red cells of the rabbit, and another which would attach itself to the red cells of the hen, and a number of complements normally present in guinea-pig's blood. When the red cells of either species were introduced into the mixture, solution would occur. It appears, therefore, that besides the complement which is capable of anchoring the amboceptor, specific towards rabbit's blood, there must be another whose haptophoric groups are capable of binding the complementophile groups of the amboceptor specific for hen's blood. Such appearances have been noted and have been dealt with. Now the red cells of the second species are added. Since no solution takes place, it follows that the amboceptors of the two haemolysins are possessed of

¹ Buchner, *Münch. med. Woch.*, No. 9, 1900; *Berl. klin. Woch.* No. 33, 1901.

² Bordet, *Annal. de l'Inst. Pasteur*, May, 1901.

identical cytophile groups, and therefore both series were anchored to the cells first introduced. Analogous conditions have already been mentioned. It appears, therefore, that Bordet's last argument is not of much value. He³ also brought forward another experiment. A guinea-pig was injected with rabbit's blood. Its serum, therefore, could dissolve rabbit's red blood cells. After being rendered inactive by heating, it could be rendered again active by the addition either of normal guinea-pig's or of normal rabbit's serum. He argued that each serum possessed its own alexin, and that the *substance sensibilisatrice* merely prepared the red cell for alexin action. Carrying the experiment further, he produced an antiserum in a rabbit by injecting the guinea-pig's serum. This serum contained chiefly antialexin, and its action was only present toward the alexin of the guinea-pig's serum, but failed entirely against the rabbit's alexin. There was also a slight diverting power toward the alexin of pigeons, which pointed to Bordet's contention against the absolute specificity of the alexins. He argued that against each alexin an antialexin could be set up which protected the sensitized red cell against the action of the corresponding alexin. Ehrlich and Morgenroth tested this, and arrived at results incompatible with Bordet's views.

Ehrlich and Morgenroth further investigated the behaviour of the inactive immune serum, and found that ten times the quantity was required to dissolve a given quantity of rabbit's blood cells when complemented by rabbit's serum, as compared with the quantity required when guinea-pig's complement was used. According to Bordet, this would mean that the blood cells, in order to be prepared for the alexins of rabbit's serum, would require ten times as strong a sensitizing as it would for the alexin of guinea-pig's serum. This is a highly improbable arrangement, but if true the ratio 10 : 1 should be constant. This is not so, and the two investigators found a ratio of 3.5 : 1 in an analogous experiment. Buchner⁴ and M. Wilde report a series of experiments intended to prove that no specific action can be ascribed to the amboceptor. They experiment with various haemolytic serums, and attempted to carry out saturation experiments. Having determined that 2 c.cm. of the serum of a rabbit treated previously with ox blood was just capable of dissolving 1 c.cm. of a 20 per cent. dilution of ox blood cells, they attempted to determine what quantity of inactive serum must be added to 1 c.cm. of the active serum in order to obtain various degrees of solution. They found that 2.5 c.cm. of inactive serum produced the greatest quantity of solution, while 5 c.cm. produced less. In the cases of the serum of a rabbit treated with dog's blood and that of a second dog active towards guinea-pig's blood, the largest amount of heated serum added gave the greatest degree of solution. In no case is complete solution reported. In the first case the addition of a greater excess of amboceptors to half the dissolving dose of complete haemolysin produces less action than the addition of a smaller excess. The available amount of complement suitable for the lysis action must be limited in the active serum, and therefore the larger the quantity of free amboceptors the larger will be the amount of complement attached to these. The fastened amboceptors find less complement for themselves in proportion to the amount used by the free amboceptors. Max Neisser and Wechsberg⁵ (loc. cit.) apply this argument to another condition.

Stereo-chemical Combination.

Bordet,⁶ Buchner,⁷ Nolf,⁸ and Nicolli⁹ take exception to Ehrlich's views as to the nature of the chemical fixation of the amboceptor, as may be deduced from what has been said. They consider that between the red cell and the amboceptor (immune body) there exists only a "level attraction," as against the view that the combination is stereo-chemical. Bordet likens the haemolytic action of the serum of a guinea-pig treated with rabbit's blood to a colour experiment. If filter paper is dipped into a solution of methylene violet all the colouring matter may be extracted; the filter paper will

assume a definitely and uniformly intense colour. If, however, the filter paper is torn into strips and gradually dipped into the solution, the first strips become more darkly coloured, and those added last find no more colour to extract. Ehrlich refuses to accept the simile, but prefers to deal with the behaviour of the amboceptor of the immune serum. The arguments in favour of the anchoring of the amboceptor to the receptor of the red cell being a chemical combination have already been given. He gives extra weight to his arguments by contrasting the specific binding of these bodies to a specific binding of certain chemical bodies, showing the possibility of a selection in the binding, according to the available reagent. He instances the formation of monazo and diazo compounds from the mixture of dioxy-naphthalin and diazo-benzol.

Roux,¹⁰ Metchnikoff,¹¹ and Pohl¹² also offer objections, which have arisen partly from misunderstanding, and which partly have been disproved. In the case of Metchnikoff the objection has been withdrawn.

The writings of Müller,¹³ Max Neisser and Wechsberg¹⁴ (comprising the actions of the haemolysis of staphylococci, and of haematolysin, leucolysin, nephrotoxin, etc.), Bulloch,¹⁵ von Dungern,¹⁶ and Dönitz¹⁷ stand in favour of Ehrlich's views, and afford fairly conclusive evidence against the alexin theory.

Gruber has recently¹⁸ attacked the whole question. Some of his generalities may be passed over, to consider his criticism of Wassermann's proof of the truth of the side-chain theory. Wassermann found that the central nervous system of a susceptible animal contains a substance (receptor) which is identical with tetanus antitoxin, and showed that an emulsion of fresh brain tissue and spinal cord of a guinea-pig is capable of neutralizing the lethal dose of tetanus toxin. Now, von Behring found that if to a definite dose of tetanus toxin a sufficient quantity of brain emulsion is added to neutralize it, and some antitoxin, the animal, instead of having an excess of antitoxin, dies of tetanic symptoms. Gruber makes deductions from this fact, which, however, do not carry conviction with them. Max Neisser and Wechsberg (loc. cit.) have already pointed out that excess is just as incapable of covering toxin as insufficiency of antitoxin. In his speech¹⁹ at the Berlin Medical Society, Ehrlich met all the objections raised by Gruber, and brought strong evidence against his deductions.

Gruber, further, turns his scepticism toward the "defect" in the cells. He presumes that if the cell were damaged its nutrition must be affected, that reproduction, compensation, and over-compensation would be impossible. This is so when the defect in the molecule is very great, but when the defect is less then regeneration is possible. A fractured bone—a typical defect—does not remain ununited, and does not die, but there is a regenerative process called forth by the defect.

The second part of Gruber's criticism is less vague. He tries to explain away Pfeiffer's observations of bacteriolysis in the living animal, by presuming that agglutination had taken place, and that the clumps of bacteria had been rapidly carried away, and claims that the bacteria disappeared in this way, but were not dissolved. The best reply to this is to compare the test-tube experiments of Bordet with Pfeiffer's results. Allowing that haemolysis and bacteriolysis do take place, he partly joins the Bordet-Buchner school in accepting alexin, but denies that this is a proteolytic enzyme, but he brings forward no new facts. The experiments from which he argues in favour of the view that alexin is a single substance have recently been put to a further practical test by Hans Sachs²⁰ in Ehrlich's laboratories. Sachs found that, by adopting the method of delaying action by keeping the blood mixture at 0°C, as described by Ehrlich in the second communication (loc. cit.), in some cases, and by using the minimum temperatures for rendering the serums inactive in other cases, all these apparently irregular haemolytic actions

¹⁰ Roux, *Annal. de l'Inst. Pasteur*, 1898.

¹¹ Metchnikoff. Loc. cit.

¹² Pohl, *Annal. de l'Inst. Pasteur*, 1900.

¹³ Müller, *Centrabl. f. Bact.*, No. 29.

¹⁴ Max Neisser and Wechsberg, *Zeitsch. f. Hyg.*, vol. XXXV, No. 22.

¹⁵ Bulloch, *Practitioner*, December, 1900.

¹⁶ Von Dungern, *Munch. med. Woch.*, Nos. 20 and 28, 1900.

¹⁷ Dönitz, *Klin. Jahrbuch*, 1899: *Deut. med. Woch.*, No. 28, 1900.

¹⁸ Gruber, *Munch. med. Woch.*, Nos. 46, 47, 48, and 49, 1901.

¹⁹ Ehrlich, *Verein für inn. Med.*, December 16th, 1901.

²⁰ Hans Sachs, *Giebt es einheitliche Alexinwirkungen?* *Berl. klin. Woch.*, Nos. 9 and 10, 1902.

³ Bordet, loc. cit., 1900.

⁴ Buchner, *Berl. klin. Woch.*, No. 33, 1901.

⁵ Max Neisser and Wechsberg, *Munch. med. Woch.*, 1901.

⁶ Bordet, *Annal. de l'Inst. Pasteur*, No. 1, 1900.

⁷ Buchner, *Munch. med. Woch.*, 1900.

⁸ Nolf, *Annal. de l'Inst. Pasteur*, 1900.

⁹ Nicolli, *Revue Générale des Matériaux Colorantes*, Nos. 43 and 44, 1900.

became absolutely regular. Ehrlich's teaching, founded on intelligent deductions from a series of the most ingenious experiments, emerges from this storm of opposition stronger, if possible, than it was before.

APPLICATION OF THE THEORY.

Interesting as haemolysis is, for the present purpose it is not necessary to discuss the process any further, but merely to use it as a type for bacteriolysis. Agglutinin can also be left out of the arguments, for as far as our knowledge at present carries us, it plays no part in the process of immunity.

In considering the factors at work which produce infection, susceptibility to toxic influences, recovery, and natural and acquired immunity, one may suppose the case of an individual whose body cells are capable of functioning normally and who comes into contact with an infecting micro-organism and follow the course of events in the light of Ehrlich's researches. The bacteria gain an entrance into the body, be it by way of the respiratory passages or in any other way, are attracted to the paraplasmic tissue, and grow. They secrete a poison, which is carried off by the circulation. This poison consists of α toxin and β toxin. The toxin has to undergo certain chemical preparation before it can be used in the body. In the form in which it is secreted it attacks the various cells of the body—for example, blood, nerve, organ cells, etc. Finding suitable receptors, it anchors itself to the cells, and as soon as the toxophoric group can act, it produces a defect. There is always an attempt on the part of the cells to cover this defect by the production of an excess of like receptors. If the toxin is a virulent one and present in sufficient quantity, this attempt is but feebly carried out; the cell becomes destroyed or changed, and, if a large number of cells of vital importance are so attacked, the individual dies. But in the case of the attempt at covering the defect being more successful, a quantity of receptors are cast off and circulate as antitoxins. These antitoxins can and do divert fresh supplies of toxin which are seeking suitable receptors. The regeneration continues as long as the toxin remains anchored and active, and thus at times the production of antitoxin is almost limitless. No fresh poisoning of the tissue cells can now take place, and therefore the life of the organism is no longer in danger. This process must take place if the defect in the cells is not too great. In tuberculosis, for instance, recovery—be it spontaneous or influenced by treatment—must depend upon this process, and in long cases ending fatally one must consider that the defect in each set of cells is too complete to allow of sufficient over-production of receptors which would be necessary to neutralize fresh supplies of toxin.

Since the toxin does not exert its action immediately, but some time elapses, corresponding to the incubation period, before it produces the first defect of the cell, one must suppose that a further period has to pass before the regeneration and over-compensation has been performed and the receptors have been cast off. In this way there exists in the course of illness a pre-antitoxin stage, which is longer than the incubation period. It can be seen that the toxin acts in precisely a similar manner as the haemolytic complement. No further explanation is required to explain those very mild attacks of infective illness beyond the mention that the toxoid practically produces no destructive defect, but still does stimulate the cell to form antitoxin.

The bacteria themselves, at the time when the supply of antitoxin has prevented fresh symptoms, produce a body which acts in destroying them. Their presence in the body causes certain cells to throw out an excess of side chains, which usually are used for the reception of nutrient molecules for the cells. The excess thus produced is useless for nutritive purposes, and therefore a casting off occurs. The freed side chains are found to have a specific affinity toward certain receptor groups of the bacteria. They now appear as the amboceptors of bacteriolysin. Anchoring themselves to the receptors of the germs, they attract the ferment-like bodies (complement) normally present in the blood, and these after the lapse of a definite time dissolve the bacteria. Again there comes the question of covering the defect, but this scarcely occurs under ordinary conditions in the case of bacteria. The variations of complement and amboceptor which have been described may be present in the bacterio-

lysin, but usually the action is smoothly performed. The individual is now freed from symptoms (toxic effects) and from bacteria. In his serum, beside the antitoxin is a greater or less excess of bacteriolysin, which is capable of attacking any newly-arrived bacteria, and dissolving them.

A rational explanation of the spontaneous recovery, of the incubation period, of the effect of toxin, and of acquired immunity is thus gained.

If one follows the recovered individual a little further, one may find that after the lapse of time the antitoxin and remains of bacteriolysin disappear from his serum. Thus the individual may become susceptible again, but there is a further regulation which may yet protect him. The receptors corresponding to the haptophoric group of the toxins may no longer be present. In such a case, bacteriolysin may be manufactured and the bacteria got rid of in this way, without any disease symptoms having appeared. The same condition is probably the cause of natural immunity in most cases, but Ehrlich²¹ has recently pointed out that antitoxin can arise without a previous introduction of toxin into the organism. In this case one must suppose that certain cells—molecules—have the habit of producing more receptors than are required for the nutrition, and that the excess of these are cast off, and according to the formation of their atom groups, act as antitoxin toward various toxins. In one of these two conditions the requirements for natural immunity are found.

THE EPIDEMIC OF SMALL-POX.

LONDON.

The epidemic of small-pox in London has begun to show signs of abatement. The following table shows for the four weeks ending April 12th the number of cases admitted to the hospitals of the Metropolitan Asylums Board and the number under treatment on the last day of each week:

Week Ending	Admissions.	Under Treatment.
March 22nd	449	1,568
March 29th	389	1,526
April 5th... ..	376	1,522
April 12th... ..	274	1,437

The number of cases under treatment at midnight on April 16th-17th was 1,410.

ESSEX.

The epidemic in Essex does not show any signs of diminishing. The following table shows the number of fresh cases for the four weeks ending April 12th:

Week Ending	Fresh Cases.
March 22nd	40
March 29th	64
April 5th	60
April 12th	62

THE TREATMENT OF CONTACTS.

Dr. Collingridge in his report, as Medical Officer of Health for the City of London, for the four weeks ending March 15th refers to a letter issued by the Local Government Board which confirms the advice he had previously offered as to the proper method of dealing with persons occupying houses where a case of small-pox had occurred. The Board considers that under ordinary circumstances it is not necessary, provided that proper precautions be taken, for such persons, other than those actually suffering from the disease, to be detained in quarantine. The precautions recommended consist in the removal of the actual patients to hospital, the disinfection of the dwelling and all articles in it that have been exposed to infection, including the clothes worn by the other inmates, and the immediate vaccination or revaccination of the latter. The persons exposed to infection are, further, to be kept under medical supervision for a fortnight and are to be examined with especial care at the end of the second week with a view of detecting possible signs of the disease. An arrangement of this sort, which interferes with the liberty of the individual as

²¹ Ehrlich, *Schutzstoffe der Blutes, Versam. Naturforscher und Aerzte*, Hamburg, 1901.