Special nursing. Inadvertently the skin was oiled by sister. Eleven other cases in the ward ; 2 protected, 9 unprotected. No secondary cases.

Eighth case.—Bed 1 : Fifth day ; pustules and scabs. Eleven other cases in the ward ; 7 protected, 4 unprotected. Special nursing. No secondary cases.

Ninth case.—Bed 1 : Sixth day ; pustules and scabs. Ten other cases in the ward ; 1 protected, 9 unprotected. Special nursing. No secondary cases.

Tenth case.—Bed 1 : Sixth day ; pustules and scabs. Ten other cases in the ward ; 2 protected, 8 unprotected. Special nursing. No secondary cases.

Eleventh case.—Bed 1 : Fourth day ; pustules and scabs. Ten other cases in the ward ; 7 protected, 3 unprotected. Special nursing. No secondary cases.

Twelfth case.—Bed 1 : Fourth day ; pustules and scabs. Six other cases in the ward ; 3 protected, 3 unprotected. Special nursing. No secondary cases.

Thirteenth case.—Bed 1 : Fourth day ; fresh vesicles, but not in ward. Eleven other cases in the ward ; 5 protected, 3 doubtful, 3 unprotected. No special nursing. No infection.

Fourteenth case.—Bed 1 : Fourth day ; pustules and scabs Three other cases in the ward ; 1 protected, 2 unprotected. No special nursing. No infection.

Fifteenth case.—Bed 1 : Fourth day ; vesicles and pustules profuse. No fresh lesions in ward. Ten other cases in the ward ; 4 protected, 6 unprotected. No special nursing. No infection.

Sixteenth case.—Bed 1 : Third day ; vesicles and pustules. No fresh lesions in ward. Seven other cases in the ward ; 4 protected, 3 unprotected. No special nursing. No infection.

Seventeenth case.—Bed 1 : Third day ; vesicles ; fresh vesicles next day. Eleven other cases in the ward ; 3 protected ; 8 unprotected. No special nursing. No infection.

Eighteenth case.—Bed 1 : Third day ; vesicles and pustules profuse. No fresh lesions in ward. Eleven other cases in the ward ; 4 protected, 7 unprotected. No special nursing. No infection.

" Special nursing " means that the senior nurse on day or night duty was detailed off to look after the chicken-pox case, and was not allowed to touch any other patient except protected ones, and no other nurse was allowed to touch the chicken-pox patient or anything connected with him. At first we admitted chicken-pox patients to the ward in the earliest obtainable stage of the disease, and although the resultant cross infections were less than one would have anticipated in an ordinary ward we felt afterwards that it was unsatisfactory to admit chicken-pox in its earliest stages. However, from observations made by us before the opening of the ward we had thought that chicken-pox did not remain infectious so long as was generally supposed. Therefore, as will be noted in the list of cases, we commenced later on admitting chicken-pox at a more advanced stage of the eruption, with the intention of working backwards in order to find the earliest period of the disease at which we could place it safely in the ward. No cross infection occurred, although the last three cases of the series were admitted to the ward as early as the third day of the eruption, and in these no special nursing was employed.

We strongly protest against any deductions being drawn from lists of different infectious diseases treated in the same ward unless the days of disease upon admission to the ward and the ages of the patients are clearly stated, and, when it can be verified, the number of protected and unprotected individuals.

As the result of our experience we feel we can assert that we could treat these infectious diseases in one ward, almost certainly, with perfect safety were we to select the day of the disease on which to admit them. We are in some doubt as to the conclusions to be deduced from our experience, but we feel satisfied that the treatment of the above diseases is more satisfactorily carried out in this class of ward than in a cubicle ward—that is, rooms with incomplete partitions between the patients. It is open to perfect supervision by the sister and senior night nurse, everything that is done can be seen by the staff, and patients frequently comment on the routine. For the treatment of diseases when they are not conveyed by air such a ward as ours is also possibly better than box wards (rooms with complete partitions). It must not be lost sight of that the ward is a thoroughly well-ventilated one, and ample space is allowed for the patient. We have no experience of ill-ventilated or overcrowded wards, and consequently our chief deductions do not refer to any other conditions than those obtaining in our own particular ward.

We think our evidence in the case of scarlet fever goes somewhat strongly to show that the infection is probably not air-borne. The evidence as to whooping-cough is less definite and we are in some doubt as to whether it may be occasionally air-borne or not. It is to be noted that the whooping-cough infections occurred in summer, when the ventilation was even more free than in winter. We think it fair to assume that the infection was not carried by the staff, at least not in each instance, for had negligence been occurring cross infection of scarlet fever most probably would have arisen also.

From our experience in this and other wards we believe that the infection of measles is probably air-borne early in the disease, but that the power of infection soon passes. We are inclined to think that the infection of chicken-pox is air-borne early in the disease, but our experience goes to suggest that on and after the third day it is probably not air-borne: in our view this probability is the most interesting outcome of the work. For many years we have held that diphtheria infection is not air-borne. No cross infections arose from German measles or from mumps, but the small number of cases treated scarcely warrant any definite conclusion. On the whole, however, from this and previous experience in other wards, we tend to the view that they are probably not air-borne.

In conclusion, we wish to say deliberately that we would rather place a child of our own into this ward, as it is conducted, than into any other ward in the hospital.

THE EXPERIMENTAL PRODUCTION OF PURPURA IN ANIMALS

BY THE INTRODUCTION OF ANTI-BLOOD-PLATE SERA.

A PRELIMINARY COMMUNICATION.

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DURING the past few years a considerable amount of attention has been directed to the part played by the blood platelets in the process of blood coagulation and to the significance of abnormal blood-plate counts in those clinical conditions which have been grouped under the general heading of the Hæmorrhagic Diathesis. Opinion has been growing steadily that the function of the blood plates in maintaining the normal coagulability of the blood by supplying an indispensable thrombogenetic element may be an all-important one, and that any derangement of that function, as manifested, for instance, by a much reduced plate content, is liable to be associated with purpuric lesions, delayed blood clotting, and the like. The

experiments recorded in this note carry the matter to a further stage, inasmuch as they demonstrate the possibility of reproducing at will the purpuric condition in animals, and consequently afford a ready means for the obtaining of suitable material for further studies connected with the etiology and therapeutics of the condition.

Experimental Data.

In the course of some work, the primary object of which was to determine whether phagocyted blood plates might simulate certain forms of cell inclusions, an anti-blood-plate serum was prepared. Blood plates were obtained by the usual method of fractional centrifugalisation of citrated human blood, and almost completely freed from admixture with red cells. The deposit of plates was finally washed in physiological saline and inoculated intravenously into rabbits in a series of successive doses. The serum of the immunised rabbits was found to contain agglutinins for human blood plates and also for human red cells, as Cole (1908) had previously shown. In the presence of this anti-plate serum phagocytosis of blood plates took place, but the serum did not appear to be very powerful in this direction, and it was felt that another system might be employed with advantage.

The difficulty of obtaining a sufficient amount of fresh human blood from which to isolate blood plates in any quantity rendered it impossible to effect an intensive immunisation of the animals. Resort was therefore had to guinea-pig blood plates. By a fortunate circumstance guinea-pig blood could be obtained in large quantities, as over 100 animals are killed in the Institute every week for another purpose (viz., the routine testing of milk for tubercle bacilli). The blood obtained from 20–30 guinea-pigs (160–250 c.c.) was received into 2-3 times its volume of 1 per cent. sodium citrate in physiological saline. The whole mass was centrifuged for a period just sufficient to throw down the red cells and leave a cloudy supernatant fluid. This upper fluid, which contained the blood plates with a slight admixture of red cells, was then removed and centrifuged completely, yielding a white deposit. The latter was then freed from red cells as completely as possible by fractional centri-fugalisation and used for the immunisation of rabbits.

It may be noted that from 20-30 guinea-pigs a yield of about 0·5-1 c.c. volume of white blood-plate deposit was usually obtained. At each inoculation the rabbit received either the half or the whole of this amount in saline suspension. Seven to eight injections were given intravenously at intervals of 6-8 days. The animals bore the injections well.

Action in vitro of the Antiplate Serum.

Guinea-pig blood plates were almost instan-taneously agglutinated by the antiplate serum in high concentration, and definite agglutination was observed in a 1 in 128 dilution of the serum. Guinea-pig red cells in saline emulsion were also intensely agglutinated by the antiplate serum, and definite agglutination occurred in a 1 in 2048 dilution of the serum.

It has to be observed that, in testing agglutina-tion of red cells, blood plates are always present in the emulsion, and it has still to be determined how far the intense agglutination of red cells is due primarily to agglutination of the blood plates with subsequent mechanical entanglement of the red cells. Whether the action on the red cells is primary or secondary may be a point of great im-portance when we come to consider the action of the antiplate serum in vivo. In a hæmolytic system, each tube of which contained 0·5 c.c. ambo-ceptor dilution (inactivated antiplate serum), 0·5 c.c. complement (guinea-pig serum 1 in 10), and 0·5 c.c. guinea-pig red cells (2 per cent. suspension), immediate agglutination of the red cells occurred in the higher dilutions of the amboceptor, and there-after lysis of the agglutinated cake of red cells pro-ceeded slowly. Complete lysis of the cake did not occur in any tube, but grades of partial lysis occurred after standing 24 hours in tubes con-taining amboceptor in dilution of 1 in 128. The effect was in marked contrast to that obtained by an ordinary anti-guinea-pig red cell serum, which gave complete lysis in the higher dilutions of ambo-ceptor without obvious antecedent agglutination.

Toxic Action of the Antiplate Serum.

The action of this serum in vitro was so striking that it was determined to test whether any toxic effects occurred in vivo.

Intravenous inoculation of the serum.—A guinea-pig of 300 grm. weight was given 1·5 c.c. serum in the jugular vein. It recovered easily from the slight operation and appeared quite active for a time. At the end of an hour and a half, however, the animal was found collapsed and death took place. Post mortem some free blood was found in the peritoneal cavity and on the surface of the liver. The blood had a reddish-brown tinge and was some-what grumous. Blood from the heart emerged as a purplish granular fluid, and it was readily demon-strated that the red cells were completely agglu-tinated. This blood clotted quite normally, but the clot showed little tendency to retract.

Intraperitoneal inoculation of the serum.—A guinea-pig of 500 grm. weight received 1 c.c. of antiplate serum intraperitoneally on May 8th. About an hour after the injection the animal became sluggish and did not move readily on excitation. On the following morning (May 9th) it had quite recovered and it remained well on the 10th, but on the 11th it was found dead. Numerous subcutaneous hæmorrhages were found in the abdominal wall. The peritoneum contained free blood, and there were extensive hæmorrhages in both tunicæ vaginales. The blood from the heart had a purplish granular appearance as in the previous animal.

Subcutaneous inoculation of the antiplate serum —This method, which yields the most striking results, has been employed repeatedly, and the picture obtained is almost invariably the same. A subcutaneous inoculation in the groin of 1 c.c. of the serum gives rise on the following day to a hard subcutaneous swelling extending to the centre of the abdomen. On the next day the swelling has extended to the lower part of the sternum, and on the third day to the neck. As a rule the subcu-taneous swelling becomes softer as the disease pro-gresses. Purpuric spots have been noted on the external skin after parting the hair in white animals. The animals usually die on the third or fourth day. Post mortem one finds an extensive hæmorrhagic infiltrate over the front of the abdo-minal wall. Numerous petechiæ are present in other remote parts—viz., on the under surface of the skin, the lungs, diaphragm, epicardium, and intestinal serosa. In one animal, which received the dose of serum subcutaneously in the dorsal region, the skin on reflexion was found to present

an enormous number of hæmorrhages of all sizes simulating exactly the purpuric condition, and internally an enormous hæmorrhage was found in the mesentery of each Fallopian tube. The lymph glands in these animals have a bright red appearance and are consequently striking objects, while the spleen shows some enlargement and turgidity. The adrenals are quite pale, and the liver has a yellowish colour. The blood in the heart, if examined immediately after death, always presents a pale granular appearance, which is due to complete agglutination of the red cells.

Another interesting feature which these subcutaneously inoculated animals show is a form of cataract (double). This condition has been noted a few hours before death, and in animals which have died during the night the condition has been almost invariably observed post mortem. The isolated lens in these cases shows what might be described as a cup-shaped peripheral opacity, but at present a full description of this interesting condition must be withheld, as it is still the subject of study.

Systematic blood counts have not yet been made in the course of the disease, but isolated observations reveal a progressive fall of the red cells, counts as low as a million and a half being recorded. Numerous nucleated red cells also appear, and large swollen megalocytes. It is proposed to study fully the changes in all the cellular elements. The pathological histology of the organs, and particularly of the hæmopoietic system, promises to be of great interest, but so far it has only been touched. Examination of the red lymph glands on stained films shows numerous free red corpuscles generally collected in clumps and numerous micro- and macrophages stuffed with ingested red cells. Similar cells are seen in the spleen and also in the material from the local hæmorrhagic infiltrates. It is therefore clear that the red corpuscles which are agglutinated by the antiplate serum, either primarily, or secondarily through the mediation of the agglutinated plates, are removed by the lymph channels from the extravasation areas to the lymph glands, where they are further broken down.

The actual mechanism of the hæmorrhage may, it is hoped, find solution with further study of the lesion in all its stages. The agglutination of the red cells has constantly been observed in specimens of blood obtained by pricking the ear of animals during the second, third, and fourth days of the disease. The blood on emerging from the ear has a granular appearance, and when placed on a slide and gently agitated settles out into large red flakes. Clotting is delayed, and there is little tendency for the clot to retract. In several cases during the later stages of the disease it has been found extremely difficult to stop the oozing from the small puncture in the ear vein. A study of the coagulation time of the blood at all stages is being undertaken.

General Discussion.

The fact that a condition resembling purpura hæmorrhagica and presenting other features associated with the hæmorrhagic diathesis can be produced in animals by inoculation with an antiplate serum adds a further link in the chain of evidence connecting the blood plates with the phenomenon of blood coagulation, and with some of the derangements of that mechanism as manifested in the various types of the hæmorrhagic diathesis. A full discussion of the important rôle played by the blood platelets in the process of blood coagulation will be found in the careful experimental study of this subject by Bordet and Delange (1912). The properties of antiplate sera have been studied mainly from the serological point of view by various authors—Marino (1905), Cole (1908), Chevrel and Roger (1907), Le Sourd and Pagniez (1908), Sacerdotti (1908), Stschastnyi (1909), and others. Much of their work has been undertaken with the view of establishing the specificity of these sera for blood plates, and the matter cannot yet be considered as settled. In this connexion it may be observed that an absolutely pure antigen cannot perhaps be obtained, and consequently the demonstration of specific properties in the antiserum can rest only on a quantitative basis. Further research is needed on this aspect of the question.

With regard to the action of these sera in the body Le Sourd and Pagniez, who worked with antisera to rabbit platelets (immunisation of guinea-pigs with rabbit plates), found that intravenous injection of the sera into rabbits led to a disappearance of the blood plates from the circulation. This disappearance lasted for 24–36 hours, but ultimately the plates returned to normal proportions. During the phase of absent plates the blood clot showed no tendency to retract, but the retractility returned with the return of the plates.

It must be noted that a very transitory fall in the number of plates in the circulating blood can be produced by the injection of other antisera—e.g., ordinary hæmolytic sera—and even normal sera. According to Le Sourd and Pagniez, after injection of hæmolytic serum the plates returned in half an hour. It is further claimed by Achard and Aynaud (1908) that the injection into the blood of various colloidal substances, such as electrargol, egg albumin, egg lecithin, &c., may cause a temporary disappearance of the blood plates.

Le Sourd and Pagniez were unable to show that their antiplate sera had any appreciable toxic action; and Sacerdotti, who worked with antisera obtained by immunising rabbits with dog blood plates, found that the serum was not toxic for dogs except in large doses and in young animals. It is highly probable that the sera with which these authors worked were not strong enough to show toxic effects or to produce lesions at all similar to those described in this communication. The total amount of rabbit plates used by Le Sourd and Pagniez throughout the whole course of immunisation of the guinea-pig was only that derived from 250–400 c.c. of rabbit blood. However, one cannot generalise from an ascertained effect on guinea-pigs to a probable similar effect of a powerful antiplate serum on rabbits or dogs. This question must be left for further research.

Finally, mention should be made of the work which has been done on the variations in the plate content in various forms of purpura in man, and in this connexion I may refer to the work of Duke (1912), who made a study of the blood plates in 31 cases of hæmorrhagic disease. Of these cases, 17 had normal or slightly increased counts, while 14 had very low counts (below 65,000 per c.mm.). His general conclusion was that when the plate count descends below a level of 60,000 there may be an abnormal tendency to bleed (as measured by the time taken for the blood to stop flowing from a cut in the ear lobe); when the count descends below 10,000 this tendency is always present, and when below 1000 it is present in its most severe form. The observation of

Le Sourd and Pagniez, that during the stage of absent plates the blood clot does not retract, was confirmed by Duke in the human cases, and supports the original statement by Hayem that blood freed from blood plates does not retract.

Conclusion.—A condition resembling purpura and presenting other features of the hæmorrhagic diathesis can be produced in guinea-pigs by inoculation of an antiserum prepared by immunising rabbits with guinea-pig blood plates.

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TUBERCLE OF THE CRUS CEREBRI SIMULATING ENTERIC FEVER.

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THE diagnosis of enteric fever in its early stages is so difficult and such a constant source of anxiety both to the general practitioner and to those in charge of isolation hospitals, and the number of conditions which may be mistaken for it by competent observers is so numerous, that it should be worth while to record some particulars of a comparatively rare condition in which the earlier manifestations presented a clinical picture very difficult to distinguish from enteric fever.

This case, moreover, is one of a considerable number coming within the scope of my own recent experience which illustrate the danger of placing too implicit reliance on the Widal reaction in diagnosis. Without minimising its value when properly applied one is justified in pointing out that it is a method in which the personal equation is very considerable, and I have known more than one doubtful case in which discrepant results were recorded by different observers. I have also had charge of a number of cases in which a "positive" reaction was unassociated with any clinical evidence of the disease in its later stages. Not all of these were ambulatory cases, for several of them developed in other and quite definite directions. The simple process of taking a blood tube and examining it or sending it away to be examined must not be allowed to become an easy substitute for careful and accurate observations of the purely clinical aspect of the case, and I am inclined to the belief that a "positive" result should only be regarded as conclusive if it occurs in considerably higher dilutions than those with which many observers are satisfied.

CASE 1.—The patient a girl aged 20, was notified to me as suffering from enteric fever and admitted into the Wigan isolation hospital on May 8th, 1912. She was a well-nourished girl and worked in a cotton mill, but was somewhat anæmic when admitted. Her home conditions were bad, and she came from an insanitary house in an area from which several cases of enteric fever had recently been notified. There was a history of a week's illness with continued fever, constipation, distended abdomen, and foul tongue. An examination of the blood had given a "positive reaction," dilution not stated. Throughout her illness headache had been a marked feature. Her temperature on admission was 100° F., her pulse 80, regular and normal in volume and frequency. Her respirations, however, were 28 per minute, and continued throughout her illness to show a frequency out of proportion to that of the pulse, only occasionally dropping to 20, and never below that.

The abdomen was slightly distended, but not more so than might be expected in view of the constipation which was present. There were no spots. The splenic dulness was increased, but the spleen was not palpable. The tongue was uniformly covered with a light brownish fur, the teeth were defective, and the breath most offensive. A further blood examination showed that there was no clumping in dilutions above 1 in 40, and as it was found that the patient had been in the hospital a year previously with an undoubted attack of enteric fever the doubtful results of the blood test could be ignored. The bowels were evacuated by an enema, and the result was a well-formed normal-looking motion. She complained of intense persistent bilateral frontal headache, but had no other symptoms, and took a fairly liberal diet quite well. She had no cough, but there was a small area of slight dulness and increased vocal resonance immediately below the right clavicle. The urine was normal in quantity and quality.

On the day following admission the headache was much better, and this improvement was maintained, but the temperature fluctuated within a few decimal points of 100°, without definite morning remissions. On the afternoon of her fourth day in hospital the nurse noticed that the girl's left pupil was dilated, and two hours later, at 5 P.M., she had an epileptiform convulsion. This passed off after a few minutes, but left her with the pupil still dilated and homonymous diplopia which lasted for five hours and then disappeared. By the next morning her temperature had fallen to normal, she had no headache or diplopia, and felt very well, but the dilatation of the pupil persisted, and there was no reaction either to light or convergence. An examination of the fundus showed nothing abnormal. She remained in this condition for three days, with the temperature oscillating quite irregularly between normal and 100°, the pulse averaging 96, and respirations 24. But on the eighth day after admission the diplopia reappeared and persisted throughout the case. I found that on the left side the image was displaced downwards and to the right, there was complete loss of convergence, the other ocular movements were limited, and there was already slight proptosis. The temperature took on a definitely hectic type, with regular morning remissions, but not rising above 101°. Antisyphilitic remedies were freely tried, but without any effect.

On the sixteenth day after admission there was marked weakness of the right hand, with some tremor, and the headache returned. From this period the symptoms developed very rapidly. The right hand became completely paralysed, and the paresis gradually extended upwards to the forearm and arm, with characteristic tremors. Before paralysis was complete the arm if extended was dropped in a series of jerks. Oculo-motor paralysis on the opposite side became complete, with marked proptosis. The headache returned and persisted;