5 francs. The majority of the cases, however, according to the reports, seem to have benefited, and probably the most striking effect of the vaccine has been the rapid manner in which it appears to have relieved pain in cases of arthritis and orchitis. Whether it will always act in this way in the hands of other workers remains still to be seen. Several cases of a similar nature have cleared up as rapidly after the injection of antimeningococcal serum.

Another feature is the ease and rapidity with which ophthalmia cleared up, but a sufficient number of cases have not yet been recorded. If it proves to be a constant character of the vaccine, we have a very potent weapon with which to combat a disease which, as a nation, we are endeavouring to control.

An interesting question is how far the cases of urethritis as reported cured are actually infection-free or whether the disease has merely been rendered latent. This is a point not brought out in the cases recorded.

As regards the fluoride vehicle, I doubt if it can have much effect in reducing toxicity. Lately I have been preparing vaccines in this way, and have found that the focal and general reactions respectively have been as marked as those produced by the injection of autogenous vaccines prepared by one of the older methods. In any case there is one objection to the use of fluoride solutions where rapidity of preparation is an essential. Gonococci, according to the authors, are only killed after forty-eight hours' exposure to the solution in an ice chest, and the length of time necessary to sterilize a given organism depends on the temperature and the species, but it depends also on the concentration of organisms in the vaccine. I find that the greater the number of organisms present per cubic centimetre the longer is the exposure necessary to effect complete sterilization. For instance, a vaccine containing 1,600 million of staphylococci per cubic centimetre still gave a growth after six days' exposure at room temperature. In such cases, therefore, we must adopt one of the older methods for the sterilization of the preliminary doses at any rate. As regards the constituents of the vaccine, the toxicity of one of them, the gonococcus, is said to be reduced in the manner described. But this organism represents only one-tenth of the total number of organisms present, since there are only 25 million present in each dose.

Moreover, while the synococcus provokes no reaction on inoculation, according to Nicolle and Blaizot, it nevertheless possesses the same curative action as the gonococci themselves. If this be so it seems at first sight unnecessary to go through the elaborate process of reducing the toxicity of the gonococci proper when present in such small number or even to include them at all.

What exactly the "synococcus" is, and what relation, if any, it bears to the gonococcus proper, is not clear, but the suggestion is that in gonorrhoea we are dealing not with a single strain but with a group of organisms all more or less related to one another—not at all an unlikely thing. On the other hand, the synococcus may be related in no way to the gonococcus proper except in so far as their symbiosis may modify the course of the disease. In other words, one must take account not merely of the main causal organism but also of other organisms in symbiosis which may considerably modify its effect and character. It would be interesting to know if the authors have used the gonococcus alone after modifying its toxicity in the method they advocate and in the same doses, and if the same effect could not be got in this way, leaving out altogether the synococcus.

These are some of the questions that arise in connexion with this preparation. Meanwhile, one must remain sceptical until a sufficient number of cases can be investigated and a little more of scientific value is known about the vaccine. This ought to be a matter of a short time only since there are no contraindications to its use, and the administration can easily be carried out by the general practitioner, no special bacteriological knowledge being necessary for its proper control. As for the route by which it is administered, it would appear from the cases recorded that it may be given either under the skin, into the muscles, or directly into a vein. Contrary to what the authors say, subcutaneous inoculation may be painless, intramuscular injections may be followed by severe pain, while no ill effects seem to attend intravenous inoculation.

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BLOOD PLATELETS IN THE TREATMENT
OF DISEASE.

By LYN DIMOND, M.B.VICT.,

LATE PATHOLOGIST AND BACTERIOLOGIST, ROYAL SOUTHERN
HOSPITAL, LIVERPOOL.

(Preliminary Note.)

THE employment of blood platelets together with the plasma in which they are suspended has given such very satisfactory results in the treatment of a large variety of morbid conditions that I think it well to publish this short preliminary note upon the methods of preparation, the technique, and results of administration.

I have employed blood platelets therapeutically in three definite ways. In the first the blood platelets are isolated from a person in perfect health, the absence of specific disease being determined by means of the Wassermann test, and of tuberculosis by means of von Pirquet's cuti-reaction; the platelets so obtained are used parenterally in varying amounts according to indication, in order to reinforce the powers of the body against the different local and general diseases due to bacteria.

In addition to satisfactory clinical results following the administration of blood platelets, determinations of the opsonic and phagocytic index, quantitative agglutinin tests, as well as complement deviation reactions, indicate that after each of such injections there is a very marked rise of the antibody content of the blood.

The different immunity reactions applied to the platelets and their containing plasma, more especially when applied thereto after recovery from microbic disease or after preliminary vaccine injection, indicate that they contain a very large part of the different antibodies produced in response to bacterial invasion of the organism. In addition to germ-caused diseases, the exhibition of blood platelets has been found satisfactory in cases of deep-seated hæmorrhage, such as hæmoptysis, hæmatemesis, and renal hæmorrhage.

A second way in which I have employed blood platelets therapeutically in the treatment of bacterial disease has been as follows:

The specific organism is isolated from a patient and with a vaccine made therefrom a healthy friend receives several injections until the various opsonic or agglutinin reactions indicate that this person's serum has a high antibacterial content to this particular organism. The blood platelets and their plasma are then obtained and used in the treatment of the original case. The employment of stock instead of autogenous vaccines has also given good results and effects a considerable saving of time. I have also used platelets isolated from patients who have passed through an attack of bacterial disease, such as those due to staphylococci, streptococci, and pneumococci. In such cases I have made the opsonic index my guide and have only used the platelets isolated from patients whose opsonic index is high.

A third method, used in cases in which the toxæmia is not extreme, such as chronic ulcers, furunculosis, acne, and tuberculosis, has been to sensitize vaccines obtained by isolating the organism from the patient's lesions by means of the platelets and their plasma. In addition to good clinical results obtained therewith, the completeness of the sensitization can be gathered from the very slight local reaction which follows their employment.

The usual technique I have used for the preparation of such sensitized vaccines has been to make an emulsion of the organism in as small a quantity of saline solution as possible, usually 5 c.cm. This emulsion I have generally exposed to a temperature of 60° C. for half an hour in order to kill the organisms; in certain cases that has been effected by adding 1 per cent. phenol after sensitization is complete.

The emulsion is added to the platelets, and their plasma under sterile paraffin, and exposed to a temperature of

37° C. for ten hours. The organisms are then separated and washed free of all plasma and suspended in as small a quantity of normal saline as possible. They are then preserved in amber-coloured ampoules upon ice in a refrigerator, being diluted immediately before use. I have usually standardized the vaccine immediately after resuspension in normal saline.

If the indications are to use platelets alone, they are obtained by allowing them to sediment by gravity after separation of the red and white corpuscles by centrifugalization. The white deposits of platelets which form at the bottom of each tube are then shaken up with 1 or 2 c.cm. of the plasma left in the tube after removal of the rest by means of a sterile pipette. I have generally used for a single injection the platelets isolated from 30 to 40 c.cm. of blood, and in cases of deep-seated haemorrhage where such an injection of platelets has been administered the resulting cessation of bleeding which rapidly follows has often been remarkable.

The methods of preparation unfortunately require time, labour, and the conveniences of a fairly well equipped laboratory, but the results have been so satisfactory that they more than repay one for the labour entailed.

Technique.

The plasma, with its platelets, is isolated in the following manner, with, of course, all due precautions to ensure the perfect sterility of all the apparatus, tubes, and media employed:

Sterile small test tubes 8 cm. long and 1 cm. in diameter are sterilized by pouring into them 1 to 2 c.cm. of sterile liquid paraffin, the liquid paraffin being employed in order to line the inside of the tubes, so as to prevent the platelets from adhering to the surface of the glass wall of the tube.

After a Record syringe has been sterilized by means of hot liquid paraffin, 4 c.cm. of the paraffin are retained in the syringe and all air excluded; 8 c.cm. of normal saline, containing 1 per cent. pure sodium citrate, is sucked up into the syringe, care still being taken to exclude air, as to the surface of the air bubbles the platelets tend to adhere.

When the paraffin and saline citrate solutions have reached the temperature of the body, this temperature is maintained in an incubator. The maintenance of the body temperature is advisable, as, in addition to facilitating isolation of the platelets by causing them to retain the rapid movements of their processes, which to a certain extent oppose the centrifugal forces that throw down the red and white corpuscles when centrifugalized, the moving apparently living platelets seem to give better results than after their movements have been slowed by exposure to the temperature of the air.

After a vein of the forearm or at the bend of the elbow has been made prominent by means of a tourniquet around the arm above the elbow, the needle of the syringe is plunged into the vein and 8 c.cm. of blood slowly withdrawn into the saline citrate solution. After withdrawal of the needle from the vein the syringe is slowly rotated in order thoroughly to mix the blood and saline citrate solution. The first few drops of blood are rejected, as some clotting may have taken place in the needle which would tend to destroy the whole specimen. The intermixture of the blood with the saline citrate solution of a higher surface tension seems to cause the red blood corpuscles to render up their platelets to the plasma.

The blood and saline citrate solution is then slowly syringed into the small sterilized tubes, so that it lies under the 1 to 2 c.cm. of liquid paraffin which they contain and which is at body temperature, as the tubes are kept in an incubator at 37° C. until required. In this way the platelets are not allowed to come into contact with the glass, to which the majority of platelets would otherwise adhere and consequently be lost.

These small tubes are then placed in the boats of a centrifuge, surrounded by liquid paraffin at 37° C., and with the hand centrifuge I employ rapidly centrifugalized for five minutes. The living platelets with their flagella beating the plasma to a certain extent oppose the centrifugal force, and at the end of the time stated are found floating in the cloudy supernatant fluid.

Where large quantities of platelets have to be isolated I generally employ an electric centrifuge rotated at about the same speed for the same time.

As a rule the platelets are found quite free from red or white cells; if any remain they can be separated after decantation either by centrifugalization or by sedimentation by gravity.

When the cloudy plasma has been decanted by means of a paraffin lined pipette into other similar tubes under paraffin, it is examined by the trypan red-paroleine method which I have described elsewhere for the presence of platelets and their number. The platelets and their plasma are administered by a Record syringe which has been sterilized by hot liquid paraffin, the liquid paraffin fulfilling two services—namely, sterilizing the syringe and needle and lining the piston and glass of the syringe so that the blood platelets are thereby prevented from adhering thereto.

The platelets and their plasma are drawn up from under the liquid paraffin by means of a sterile filler attached to the syringe the inside of which has previously been sterilized by hot liquid paraffin.

The needle, previously sterilized by hot paraffin, is fixed to the syringe and the contents are administered hypodermically at a convenient site, the skin at the point of puncture being previously sterilized by painting with tincture of iodine.

Though good results are obtained from small doses of platelets and their plasma, such as from 1 to 5 c.cm., I have in particular cases, according to the indications, by means of 20 c.cm. Record syringes, administered as much as 30 to 40 c.cm. directly into the connective tissues under the skin between the shoulder blades. During an experience of many hundreds of injections, varying from 1 c.cm. to 40 c.cm., I have never yet seen any untoward result apart from a slight reddening of the skin for a few centimetres around the puncture which clears up in from twenty-four to thirty-six hours. The patients have never complained of any pain as an immediate or after result of the injections, and in the majority of cases the hyperaemia of the skin is simply accompanied by a slight sensation of itching.

When vaccines are administered either with the platelets or after sensitization by means of the platelets and their plasma, more definite local signs are the result, but never so marked or so intense as when the vaccine alone is injected.

Where preliminary vaccine treatment of a donor by means of a stock vaccine or an autogenous vaccine prepared from the causal organism obtained from the patient is undertaken, I have almost invariably followed the course of the immunity reaction by means of the opsonic index, agglutinin reactions, etc., and have abstracted the blood when the index is at its highest point.

Advantage has also been taken of the cumulative action of vaccines when their dose is properly spaced. Two doses are given successively so as to raise the patient's index by successive steps to a higher level of immunity. Such accumulative action following two properly spaced doses of *Staphylococcus pyogenes aureus* can be noted in the accompanying diagram, the doses in each case being 200 million cocci at an interval of ten days.

After the administration of tuberculin the platelets are obtained during the positive phase, between the fourth and seventh day after, and in the case of staphylococci between the sixth and tenth day after.

Having been fortunate enough to be able to treat with platelets a large number of acute and chronic pulmonary conditions, as well as numerous cases of the secondary infection in phthisis, I have found that for the organisms noted below the most suitable time for isolation of the platelets is, as a rule, as follows:

<i>Diplococcus pneumoniae</i> , platelets withdrawn 5th day after injection.				
<i>Micrococcus catarrhalis</i>	"	"	3rd	"
<i>Friedländer's bacillus</i>	"	"	8th	"
<i>Bacillus influenzae</i>	"	"	2nd	"
<i>Streptococcus pyogenes</i>	"	"	3rd	"
<i>Bacillus septus</i>	"	"	6th	"
<i>Bacillus pertussis</i>	"	"	3rd	"

Regular estimations of the opsonic index in certain of these cases have shown that when the platelets are withdrawn after the above interval following the vaccine injection the best immunizing response is obtained.

I hope shortly to deal with the clinical history of my cases.

THE late Mr. Oliver H. Fowler, in practice for many years at Cirencester, left estate value £29,031.

ON account of the war the Executive Committee for the Organization of the Second Eugenics Congress has decided that it will be impossible to hold it as arranged in New York in September, 1915.