MEDICAL BLOOD PREPARATIONS

BY

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This is the first of two articles by Dr. Bogomolova, one of the delegation of Russian doctors who visited Britain last autumn as guests of the B.M.A. Her second article, on "Blood Substitute Solutions," will appear next week.

Blood transfusion as a method of treatment has become widely used in every field of medicine. Scientists, however, have not confined themselves to studying the method of blood transfusion; they have long since come near to finding means of utilizing the individual fractions of blood in treatment.

As far back as 1932 Filatov and Kartashevski, of the Leningrad Institute of Blood Transfusion, worked out the problem of transfusing blood plasma and erythrocytes, isolated from each other (Kartashevski and Filatov 1934), and plasma transfusion has now found wide application in medical practice for shock, burns, hypoproteinaemia, etc.

As is well known, blood plasma, in its turn, may be subdivided into a number of components, the so-called fractions. Each of these plasma fractions is endowed with a definite physiological activity, in proportion to which its use may be evaluated. For example, albumins are applied as a blood substitute in controlling shock. Globulin is a particularly important fraction of the plasma proteins. It is known that the concentration of immune antibodies in a purified gamma-globulin is 25 times greater than in whole blood. Fibrinogen is a protein of great physiological importance in blood coagulation.

In addition to using individual fractions of blood, it is possible to combine them and thus utilize interaction of the individual fraction. In recent years the Leningrad Institute of Blood Transfusion has produced several such preparations. The substances so obtained may be divided into the following groups: blood substitutes; haemostatics; stimulating preparations—that is, substances which accelerate the healing of wounds and sores; preparations for the treatment of anaemia; plastic preparations—that is, those required for plastic restorative purposes in surgery.

Blood Substitutes

Mention should be especially made of dried blood plasma. We have elaborated methods of storing dried plasma which enable us completely to avoid infecting patients with the virus of hepatitis. These methods consist in adding to the blood an antiseptic (tripoflavin) or sulphamides and then extracting the plasma and drying by the vacuum-freezing method (Krotova, 1952; Krotova and Depp, 1952).

The method of transfusing the erythrocyte mass, one of the blood fractions, has lately found wide application. We have proved that preserved erythrocytes can be kept for 30–40 days (Krotova, 1952).

Another preparation belonging to the group of blood-substituting media—namely, dried haemoglobin—is worth mention. Up till now it had not been obtained in a pure state, since, as a rule, a part of the haemoglobin is transformed into methaemoglobin in the process of drying. We have now worked out a method of preparing restored haemoglobin in a dry state (Andrianova, 1955). It is a red powder that contains no impurities and readily dissolves in water-

and-salt solutions. A small dose of dried haemoglobin added to the blood serum suffices to raise the effectiveness of the latter.

Haemostatics

The second group of preparations comprises those intended for local haemostasis. These include the haemostatic sponge, dry thrombin and fibrin "cotton-wool," antiseptic biological tampon, fibrin powder, and haemostatic suppositories.

Haemostatic sponge is produced from blood plasma; it is of porous structure and looks like an ordinary rubber sponge. The haemostatic sponge is very hygroscopic, and, when applied to the bleeding spot, absorbs the blood and brings about its rapid coagulation (Bogomolova, 1951). It has been proved that the sponge left in the tissues of the body during haemostasis completely dissolves.

The neurogenic factor has been found to play an important part in the mechanism of action of the haemostatic sponge. Experiments on dogs have shown that sponge mechanically occludes the bleeding vessel and causes greater coagulation of the blood flowing from the bleeding-point; it acts also, above all, on the receptor apparatus of the vascular system and causes a reflex contraction of the bleeding vessels, which is of decisive importance in haemostasis. It has been found of great use in surgery.

The latest experiments carried out at the institute have helped in elaborating a technology for the production of haemostatic sponge from the blood of beef and dairy cattle. In use, these sponges are saturated with antiseptics, and are devoid of any antigenic properties (Klement, 1955).

Dry thrombin of the Leningrad Institute of Blood Transfusion is another haemostatic preparation (Andrianova, 1952). It arrests the bleeding of injured organs and is of particular importance in closed cavities. Thrombin, in combination with fibrinogen, is used in cases of special plastic operations when a physiologically adhesive material is required. This method is particularly convenient in skin-grafting. In such cases the strip of skin is impregnated with a thrombin solution, while the site on which the skin is to be grafted is anointed with a fibrinogen (or plasma) solution. The strip is applied to the previously prepared site, on which a clot of fibrin is formed that acts as a glue.

"Cotton-wool" made of blood fibrin belongs to the same class of haemostatic preparations (Filatov, 1955; Filatov and Teodorowitch, 1954); it also dissolves. Experimental investigations have proved that "homo-cotton-wool"—that is, cotton-wool obtained from homogenous blood—may be applied for haemostatic purposes in cases of injury of the internal organs. In such cases it is recommended that the cotton-wool should be dipped in a thrombin solution.

All the above biological haemostatic drugs can be widely applied. When left in the tissues of the body they completely dissolve, without bringing about any reactions. This has been confirmed by numerous clinical observations made by various investigators.

Biological antiseptic tampons containing antibiotics, such as penicillin and streptomycin, as well as antiseptics, are recommended to stop bleeding from infected wounds. Research carried out by a number of authors has shown that when a tampon saturated with penicillin or streptomycin is introduced into an infected cavity the antibiotic slowly penetrates into the blood, as from a depot. Investigation has revealed that a medium therapeutic dose of antibiotic appears in the blood within four days (Melnikova, 1954).

One of these preparations, the antiseptic biological tampon, composed of blood plasma with gelatin, is a porous, dry elastic mass of a light yellow colour (Bogomolova and Alexandrova, 1954). It can be made in any size or shape, and is packed so that it can be used for first aid to wounded on the spot.

Stimulating Preparations

The next group, the so-called stimulating preparations, includes sterilized serum made from the blood of donors. The preparation is obtained by appropriate treatment of human blood serum, which is then subjected to repeated

sterilization in an autoclave at a temperature of 125° C. As a result of the high temperature and pressure, the serum albumin disintegrates, and a gently acting protein preparation is thus created. It is a transparent brown fluid and is supplied in 10-ml. doses (Filatov, 1953).

Clinical experience has shown that the best results are obtained with sterilized serum when it becomes necessary to improve the processes of regeneration—that is, chiefly in cases of non-healing ulcers. The sterilized serum is used when treating gastric and duodenal ulceration and other diseases. It is introduced intramuscularly in increasing doses, ranging from 1 to 10 ml. daily, the course of treatment comprising 10 to 20 injections. Up to the present the Leningrad Institute of Blood Transfusion has treated more than 1,000 cases of peptic ulcer with sterilized serum. A favourable result was recorded in 90% of these, and complete healing in 40%. No aggravation or exacerbation of the disease process was observed, and there were no reactions or complications (Filatov, 1950).

Highly interesting data were obtained when sterilized serum was used as a solvent for penicillin. It appeared that when penicillin dissolved in sterilized serum is introduced intramuscularly it becomes possible to preserve a high concentration of the preparation in the body for a much longer time, and, what is of particular importance, to increase markedly the medicinal effect of the antibiotic (Filatov, 1955).

Yet another preparation, named haemohormonostimulin (Bakscht *et al.*, 1955), has been suggested for stimulant therapy. It is made of retroplacental blood and contains valuable hormones, the introduction of which jointly with the serum is particularly effective. Haemohormonostimulin is injected intramuscularly in single doses of 40–80 ml.—or, occasionally, in repeated doses—in cases of climacteric neuroses, ovarian insufficiency, climacteric dermatoses, and other instances of hormonal disorders in women. According to our data, the results obtained from haemohormonostimulin are undoubtedly superior to those produced by the use of conventional hormonal preparations, including synthetic ones. We believe that such a positive effect of haemohormonostimulin can be explained by the fact that on its introduction there takes place a combined action of the hormones and serum of pregnant women, so rich in active substances.

Treatment of Anaemia

Various preparations made from animal blood have long been used to stimulate blood formation in cases of anaemia. These include haematogen, haemol, and other blood constituents. Since blood preparations do not by themselves produce a rapid and lasting restoration of blood in cases of anaemia, the task was to combine them with medicinal drugs. The preparations so far suggested do not, however, meet the physicians' requirements, since they produce only a comparatively slow rate of blood regeneration.

A new haemoglobin-containing preparation, called haemostimulin (Kouralava 1954), has been tried at the Leningrad Institute. It is made of animal blood with trace elements added to it. As is well known, in addition to iron, necessary for the building up of haemoglobin molecules, a number of other metals, evidently acting as catalysts, participate in the process of blood regeneration. Such metals include copper and cobalt. Owing to the happy combination of its components, haemostimulin exercises a strong stimulating influence on blood formation and is successfully employed in treating hypochromic anaemia of various aetiology. When this preparation is administered to anaemic patients the haemoglobin content rises by a daily average of 1 to 1.5%.

In a number of cases haemostimulin has rapidly eliminated anaemia when the usual methods of treatment have proved unsuccessful.

Preparations for Plastic Surgery

This group of new preparations consists of those designed for plastic surgery. The first in importance are fibrin films, made of human blood as well as of the blood of beef and dairy cattle.

Films made of human blood can be used for plastic operations in cases of defects in the dura mater and peritoneum, and to cover wounds of the internal organs. Cheaper and more easily available fibrin films made of animal blood may be used externally (Filatov and Goschkina, 1950).

The question naturally arises: are not such films harmful to human tissues, since they are made of heterogenous blood and possess anaphylactogenic properties? It is well known that foreign protein, particularly when repeatedly applied, always brings about phenomena of general and local anaphylaxis. By properly treating animal blood we succeeded in eliminating the anaphylactogenic properties of heterogenous films.

Fibrin films are elastic. This property helps one to cover evenly the injured portions of the skin, thereby protecting the bared nerve-endings from external stimulation; the flow of nerve impulses from the injured area is also eliminated—a highly important point, according to Pavlov's teaching.

Fibrin films are also transparent. This makes it possible to observe the condition of the wound without risk of secondary infection during dressing and without further trauma to the wound. They also have a great capacity for adsorption, which is highly important clinically, both with regard to the extraction of toxin from the wound and rapid drying, and with regard to the creation of bactericidal depots—impregnation with bactericides having previously been done.

The fibrin film is capable of dissolving when acted upon by micro-organisms. This property is of some importance in the treatment of burns and other skin injuries, since dissolution of the film on the infected site makes it possible to recognize infection quickly, and thus prevent its spread over the whole of the wound (Goschkina, 1954).

Impregnation of the fibrin film with bactericidal substances prevents infection from spreading on the surface of the burn. The bactericidal action manifests itself the whole of the time the film is on the wound—that is, up to the moment when the film dries.

Clinical observations in over 2,000 cases of burns have proved that the films speed up the healing of burn wounds by four to five days as compared with other methods. They have been widely used in treating not only burns but abrasions, bedsores, and other skin injuries, but also for the repair of defects in serous membranes and the integuments of the organs. Considerable clinical experience has proved the unquestionable effectiveness of the fibrin film.

Of other preparations produced at the Institute of Blood Transfusion mention should be made of bioplastics. Two types of these have been made: (1) Rapidly resolving plastics for the construction of splints for use in gastro-intestinal anastomosis. Bioplastic splints are not only designed to facilitate gastro-intestinal anastomosis, but when left in the intestines they are a source of valuable nourishing substances (Filatov and Andrianova, 1952). (2) Slowly resolving bioplastics for use as intra-osseous splints in cases of fracture.

All the suggested plastics have been tested as resolving materials in plastic surgery, and the results have been good.

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