THE EARLY USE OF PLASMA FOR TRANSFUSION

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It is an unfortunate but recognisable fact that the development of the use of plasma as an alternative to whole blood for transfusion can be related directly to World War 2. The move towards a National Blood Transfusion Service and the work of Percy Lane Oliver in obtaining civilian blood donors prior to 1945 is well documented, but the development of blood transfusion techniques and blood storage was stimulated by and developed primarily for war casualties. In 1939 the directors of the London blood depots together with the Medical Research Council (MRC) decided to standardise transfusion equipment, resulting in the introduction of the 'MRC Blood Bottle' (a modified milk bottle design!). Initially whole blood for transfusion was taken into a simple citrate-saline solution, but in January 1940 a 'glucose-citrate anticoagulant' (with a final glucose concentration of 0.3%) was introduced as a standard blood preservative. Initially this was used to store whole blood for 2 weeks, but further modifications of this solution using citric acid and disodium citrate enabled a storage time of 3 weeks to be introduced in 1943.

Unfiltered liquid plasma had been used as a substitute for whole blood in the late 1930s and had in fact been used during the Dunkirk and North Africa desert campaigns. Not surprisingly, bacterial contamination was a major problem related to the production and subsequent storage of liquid plasma donations using MRC blood bottles.

The development of plasma products for transfusion had begun in the US prior to the 1930's but was extensively expanded immediately prior to and during the involvement of America in the war. This was stimulated primarily by the geographical isolation of the USA from Europe as well as by the limited storage time available for whole blood (all supplies had of course to be shipped at that time). Following the important development of plasma fractionation techniques by Edwin Cohn, the decision by the USA's 'Blood for Britain' project was that America should supply plasma rather than whole blood for transfusion. This decision stimulated additional research and development of plasma products in the USA.

Based on work initially done during the Spanish Civil War, pooled plasma was normally used for transfusion, i.e. the plasma from ten different ABO groups (normally 4 group O, four group A and two group B or AB donations) was pooled together so as to neutralise ABO antibodies, thereby making it a 'universal donor' product. Note: the benefits of producing plasma in this way were thought at the time to far outweigh any potential increased risk of microbiological infection resulting from the pooling process. Initially, liquid plasma pools (separated from red cells by sedimentation and only later by centrifugation) were produced, however many of these batches were found to be bacterially infected and the amounts produced were small compared with the volume of whole blood donations collected and transfused by UK 'blood depots' for war casualties. However, the problem of infection led not only to developments in the sterility of anticoagulant solutions and equipment (by autoclaving) but also the production of (400 ml) bottles of freeze-dried plasma (and serum) products.

Freeze dried plasma was produced from small pool plasma obtained from blood that had time-expired or had been returned to Transfusion Centres from hospitals. The plasma from ten donations was siphoned-off into individual Winchester bottles within

a sterile room under aseptic conditions. The aim of freeze drying the plasma was to produce a stable product that could be conveniently kept for long periods without refrigeration. Prior to the drying process, each Winchester bottle of plasma was bacteriologically screened and then divided into 400 ml amounts in standard MRC bottles. Each bottle of dried plasma was produced by a process of spin freezing and desiccation. Once produced, the dried plasma could be stored without refrigeration and was reconstituted prior to use using 400 ml of sterile pyrogen-free distilled water.

The freeze drying of plasma subsequently led to the development of plasma filtration and fractionation methodologies leading to the production of dried fibrinogen products, initially at the Lister Institute, though increasing demand for these products by the 1950's led to the opening of the Blood Products Laboratory (BPL) in England.

The introduction of plastic blood packs throughout England in 1975 revolutionised blood component therapy. The ability to separate plasma from red cells using a single sterile 'multi-pack' design, centrifugation and 'plasma press' (to manually squeeze the blood pack) provided a simple, reliable and safe means of producing single donor fresh frozen plasma and cryoprecipitate donations for transfusion. This development of course also had major implications for the production of plasma pools for fractionation purposes, initially enabling sterile pooling into 5 litre packs. The production of small pool dried plasma was overtaken in the early 1970s by the production of a stable plasma protein fraction (PPF) which was heat treated (60^{o}C for 10 hours) and contained at least 90% albumin.

Bottle of DRIED HUMAN PLASMA FOR TRANSFUSION

The bottle label includes the following information: Contains the dried solids (about 20 g. protein) from 400 c.c. of pooled citrated plasma, and may be given to patients of ANY BLOOD GROUP. To reconstitute add 400 c.c. sterile pyrogen-free distilled water. Intravenous saline or glucose solutions may also be used. Reconstituted plasma MUST BE DISCARDED if not used within 3 hours

Bottle of DRIED HUMAN PLASMA FOR TRANSFUSION

Blood Products Laboratory, Lister Institute, Elstree, Herts. Batch No. 610 4722/2. Prepared: Mar 1970 / Expiry: Feb 1978. The bottle label includes the following information: Contains dried solids from 400 ml. unfiltered pooled citrated plasma. May be given to patients of ANY BLOOD GROUP – Protein 5% Citrate 1% Glucose 0.6% To reconstitute add 400 ml. pyrogen-free distilled water. To administer with a piercing needle transfusion set, replace metal cap and rubber wad and SCREW CAP DOWN FIRMLY. Reconstituted plasma MUST BE DISCARDED if not used within 3 hours. STORE IN A COOL DRY DARK PLACE.

Bottle of STERILE DISTILLED WATER FOR RECONSTITUTING DRIED SERUM AND PLASMA (400 c.c. PYROGEN-FREE)

The bottle label includes the following information: Sterilised: 8 Nov 1977. Expiry Date: 7 Nov 1978.

SMALL POOL PLASMA SEPARATION (CIRCA 1950S/1960S)
Siphoning plasma into Winchester within a sterile room using “aseptic techniques”.