INTRODUCTORY NOTES

I believed that the following 'article' was produced as a handout / lecture notes for the BTEC HNC Course in Medical Laboratory Sciences – Transfusion Science at Manchester University. I came across a photocopy of the original document, dated 1990, a number of years ago. Although no author is identified in the original document, the author is in fact Mr Peter Howell (ex Manchester Blood Centre) who ran the MLS Transfusion Science Course at Manchester University at that time.

As will be identified, the content represents a personal view of the history of the 'Blood Transfusion Service'. The original typed document is reproduced here (with permission – as originally written) for two reasons. Firstly, it contains important historical information regarding the development of the Blood Service in England that is collected together within a single document and secondly, since it was written in 1990 it gives an important insight into the roles of a Blood Centre and the organisation of the Blood Service in England at that time.

NOTE: This document has been produced for historical purposes only and should not be used as a source of current information regarding NHSBT policies or procedures. The terminology used in this document is 'of its day' and has not been changed to bring it in line with currently accepted terminology.

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THE HISTORY, DEVELOPMENT AND ROLE; PAST, PRESENT AND FUTURE, OF THE BLOOD TRANSFUSION SERVICE

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THE EARLY YEARS

In 1628 William Harvey was the first to recognise that blood circulated through the body, and a few years later, in 1647, attempts were made to transfuse animal blood into humans. The presence of anti-species antibodies in the patients, as well as the crudeness of the operation made a low success rate inevitable.

It was not until much later, in 1818, that James Blundell, recognising the need to treat women with post-natal haemorrhage transfused human blood rather than animal blood. The difficulties were enormous, and donation was either by artery to vein anastomosis or by the use of a syringe. In any event the mortality rate was very high, and quite apart from the unacceptable conditions in which the transfusions were performed, on many occasions the blood transfused must have been ABO incompatible. It was not surprising therefore that by 1900 only 347 cases of human transfusion had been recorded. The discovery by Landsteiner in 1900 that there were intra-species differences between the bloods of different humans marked a turning point in the early history of blood transfusion practice. The fact that the plasma/serum of certain individuals reacted vigorously with the cells of some other persons provided the basis of establishing the four major ABO group categories now known as A, B, AB and O. The definition of the major ABO groups has since ensured that while it may not always be possible to transfuse identical groups, at

least the donor cells should be assured of compatibility with the recipient's serum in respect of ABO groups.

The First World War saw the introduction of sodium citrate as a constituent which would prevent blood clotting and allow collection of donor blood away from the site of operation or eventual infusion, a fact which allowed the collection of blood at casualty clearing stations of the British Army prior to despatch for transfusion to soldiers wounded at the front. At about this time it was also recognised that by maintaining blood as sterile and as cool as possible, it increased its life-span "in vitro".

Notwithstanding these developments most of the blood transfusions carried out between 1918 and 1940 relied on voluntary donors who were recruited to attend at hospitals and give blood directly to patients. Voluntary donor panels formed by members of St. John's Ambulance and The British Red Cross were used principally to supply local individual hospitals with fresh blood. While the first blood bank as we would recognise it today was setup in Chicago in 1936, it was not until the start of the Second World War that the Transfusion Service as we know it today in the U.K. began to emerge. Until 1939 many transfusions were relatively crude, involving the insertion of a large needle into the donor's arm, the collection of blood into an appropriate enamel jug or container containing citrate, and the dispensing of the mixed anticoagulated blood into an open burette connected via a rubber tube and needle into the patient's arm. By 1940, however, a few Transfusion Centres had been opened in the U.K., and the organised collection of blood was beginning to take shape. Closed systems of collection and storage were being developed, and the search was on for improved preservatives. In 1942 acid-citrate-dextrose solution was introduced, and the Emergency Medical Service had by this time set up eight Regional Transfusion Centres. By the end of the war the amalgamation of E.M.S. and the Army Transfusion Service resulted in the formation of the National Blood Transfusion Service more or less as we know it today. In 1948 the Service became part of the N.H.S. and is now administered by the Regional Health Authorities.

THE EARLY ROLE OF THE TRANSFUSION SERVICE

The major role of the B.T.S. up to the mid-1960's centred around the collection and quality control of blood and its distribution to the hospitals. To this end the Centres were virtually self-supporting insofar as the anticoagulant was manufactured under aseptic conditions and dispensed in bottles at the Centres ready for blood collection. At this time, the Service provided other solutions suitable for intravenous use, in particular saline and water, the latter being essential for reconstitution of the main products, namely, dried plasma, fibrinogen and albumin, recovered by the Blood Products Laboratory from the time expired plasma despatched to this central laboratory from the Regional Centres. A large component of the work of the Service at this time involved the meticulous preparation of such solutions together with their exhaustive bacteriological, physical and chemical quality control. The major components in the collection and safe distribution of blood and blood products at this time can be summarised as follows:-

1. The organised recruitment of donors for bleeding at allocated blood donor sessions
2. The rigorous large scale ABO and Rh grouping of donors which, by 1958, included the use of O serum to identify A_4 donors and anti-E to effect the full definition of Rh negative (rr) donations
3. The limitation of transmittable disease by both the volunteer verbal screening of donors and the laboratory testing for syphilis
4. The final checking, testing and banking of the whole blood prior to distribution to the hospitals

5. The separation of time expired plasma for despatch to the central processing laboratory (B.P.L.)
6. The receipt and distribution of blood products such as dried plasma, fibrinogen and albumin

The Centres were also involved in other supportive services, of which the major ones were as follows:-

1. The large scale testing and screening of antenatal samples to help in the prediction and management of primarily Rh haemolytic disease
2. The collection of high titre anti-A and anti-B reagents, initially screened at the Centres and then sent to the Blood Group Reference Laboratory for preparation and re-distribution to the Regions as typing reagents
3. The collection of antisera; e.g. O sera, anti-D, AB serum for the selection, preparation, standardisation and distribution of additional test reagents to the hospitals
4. The investigation of referred cases from hospitals for antibody investigations, selection of compatible blood and crossmatching as appropriate

THE MORE RECENT ROLE OF THE TRANSFUSION SERVICE

Towards the end of the 1960's a wind of change began to sweep through the Transfusion Service to establish an expansive development period, which is reflected in a multitude of tasks now performed by the Centres and to some extent the more sizeable hospital blood banks. Four major factors initially influenced the enormous expansion during this period:-

1. The introduction of plastic packs for blood collection, which has revolutionised the separation of blood products enabling the implementation of specific component therapy.
2. The identification of the HBs Antigen as a marker for one transmittable agent of Hepatitis, and the subsequent development of increasingly sensitive techniques for its detection.
3. The emergence of transplant surgery and the requirements to provide a Tissue Typing service for either the provision of typed compatible organs and/or the provision of a screening service to provide suitable donors for supportive therapy for leukaemic patients or those nominated for transplant surgery.
4. The development of automated techniques with particular impact on the automated antibody screening of donor and antenatal samples and the large scale ABO and Rh grouping of donors.

While the major earlier role of the Service has been generally maintained following the introduction of plastic packs, the preparation of intravenous solutions was phased out and replaced by an expansive programme of blood product preparation. This has involved the local production of cryoprecipitate, fresh frozen plasma, fresh frozen plasma cryo-deficient, and platelet products and the collection of fresh frozen plasma in special packs, as well as cryo-poor plasma and time-expired plasma for onward transmission to the Blood Products Laboratory. This is one of two major central laboratories and is involved in the separation, fractionation and preparation of a whole range of products for re-distribution to the Regions. Dried plasma was eventually replaced by a fluid, plasma protein fraction (PPF), now defined as 4.5% albumin, and while the production of fibrinogen has been phased out fluid albumin (20%) is now produced instead of dried albumin. Other products currently produced are Factor VIII concentrate, Factor IX concentrate, and specific

immunoglobulin preparations including anti-D immunoglobulin. Thus, blood components are now produced extensively at local and national level for regional distribution to patients who require transfusion therapy to accommodate specific deficiencies.

Apart from the tests previously indicated for monitoring blood donations, it became possible to test all units to exclude the presence of Hepatitis B surface antigen using either a highly sensitive radioimmunoassay technique or more commonly a very sensitive enzyme-linked immunosorbent assay (ELISA) technique. Checks are carried out on HBsAg negative donors implicated in post-transfusion hepatitis, and positive samples, or those involving suspicious histories of jaundice, are referred to a specialised laboratory (Public Health Laboratory). National quality assessment schemes are operated to check the standards of monitoring and Regional screening. All donations are checked for atypical blood group antibodies and most Centres have a high level of automated grouping of donor samples, incorporating automated recognition of sequential barcoded donation numbers coordinated with a real-time interpretation and print-out of data. In the most sophisticated automated systems the results from the real-time testing of samples can be correlated with known data previously input and stored for comparative purposes. The use of barcoded labels has provided a mechanism for the capture of data using laser beams or light pens so that information on grouped donations can be stored and accessed to provide a high level of security in the labeling of blood packs.

More blood grouping reagents became available and, once again, the supply was carried out jointly by the local Centres and/or the National Reference Centre, originally a division of the Blood Group Reference Laboratory, but latterly identified as BPL (Diagnostics). Apart from originally producing ABO and Rh typing reagents as well as antiglobulin reagents, the BGRL serves other functions, which can be summarised as follows:-

1. The administrative maintenance of National and International Panels of donors with rare cell types
2. The provision of a red cell reference service for the further investigation of serological problems referred by the Regional Centres or from abroad, in the latter case acting in the capacity of the International Reference Centre (WHO Laboratory)
3. The distribution and monitoring of quality assessment schemes provided for internal and external quality assessment of serological work at the RTC's and hospital laboratories was originally carried out by the BGRL. Since, the mid-80's, however, this responsibility has been transferred to the National Institute for Biological Standards & Control (NIBSC).

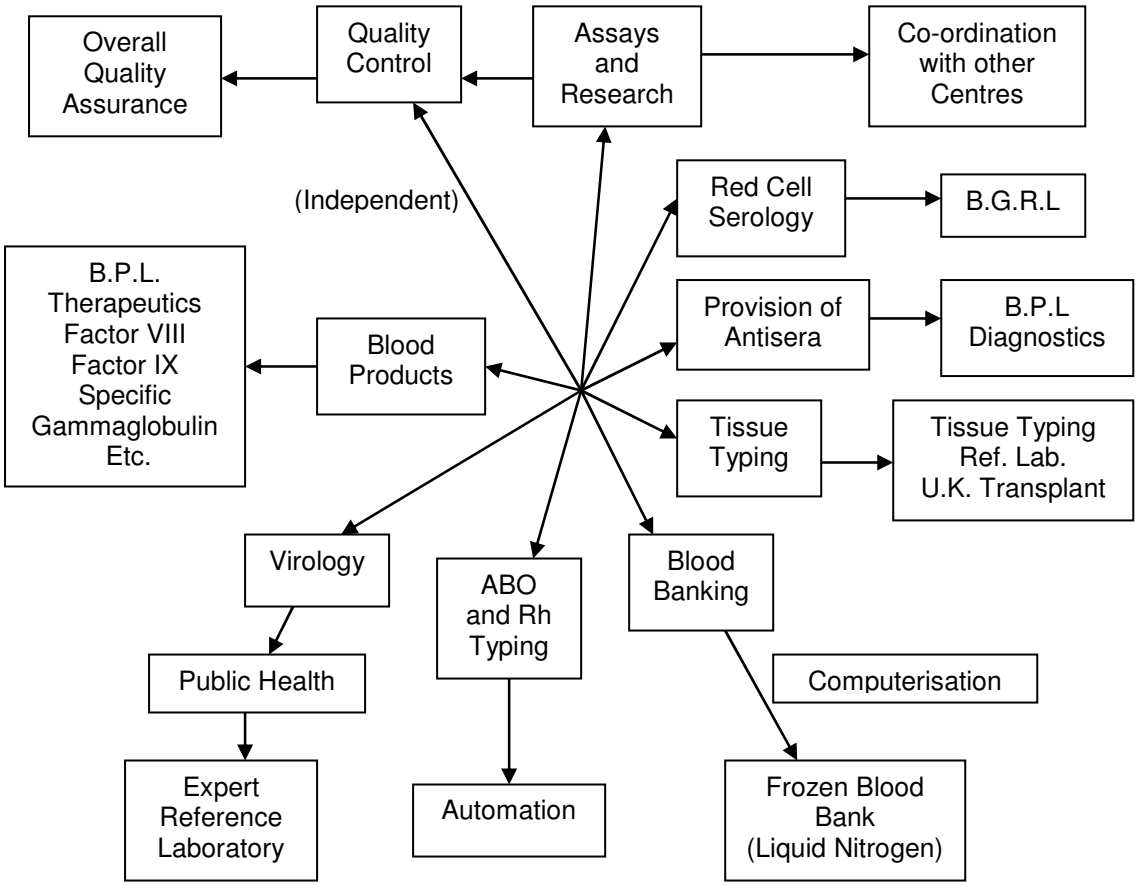
All Regions now have some form of Tissue Typing Service. This varies from those which are intimately involved in direct transplant work to those whose role is more supportive in terms of monitoring sera for HLA antibodies in prospective transplant recipients, providing extensive panels of tissue typed donors for the provision of blood components; i.e. platelets, etc., for supportive therapy, providing a screening service for prospective bone marrow transplant patients and the examination of disease associations. Once again, a specialised National Reference Laboratory provides the link-up for, provision of dedicated typing reagents, selected panels of organ donors, reference purposes and the organisation of quality assessment schemes to monitor Regional performance and reliability of testing.

As the role of the Transfusion Service has diversified, there has been a growing need to streamline the Service and concentrate effort on priority areas of work. Thus, in some Regions, much of the routine antenatal screening is now done at hospital level. The increasing level of technical expertise during the last decade, and

the introduction of automated technology in the hospitals, has made it possible for many hospitals laboratories to routinely group and antibody screen antenatal and other patients. Furthermore, some of the major laboratories can carry out some investigational work, and, hence, certain RTC's now place more priority on the investigation of special antenatal samples where antibody screening tests have been found positive and anti-D quantitation in relation to the prediction and amelioration of haemolytic disease of the newborn. Lastly, throughout its development the Transfusion Service has maintained an element concentrating solely on research and development. The development of monoclonal antiglobulin reagents, the evaluation and consolidation of new technologies and the development of quantitative methods for assessing antibody uptake on to red cells are only some of the areas presently being explored.

The internal specialisations within the Centre and the interactions with Central Reference Laboratories are summarised in Fig.1

FIG.1: INTERNAL SPECIALISATIONS WITHIN THE CENTRE



THE DRIVING FORCES OF THE 1980's

As the Service entered the 80's, the pace of technological change continued to increase dramatically initially driven by firstly, the demand for National self-sufficiency and secondly the requirement for accountability and subsequently by the impact of 'AIDS'.

The drive for National self-sufficiency has continued unabated during the last decade and has required an immense increase in resources. Whilst the earlier

targets for National production of Factor VIII stood at about 30 million units annually the aim has been to increase this to 100 million units and while it was hoped to reach this target by 1990 in fact there is still some way to go. A commensurate increase in the provision of volume expanders such as PPF (now 4.5% albumin) and albumin (20%) was also anticipated and this has largely been achieved by the increase in the use of secondary additive solutions such as SAG-M combined with extensive plasmapheresis programmes. The provision of raw plasma materials using these strategies has now reached a level of 490 tonnes of plasma annually and it is unlikely that a much greater increase is required to enable the level of manufacture needed to meet the demands of the future.

With increasing numbers and variety of products being produced, the Transfusion Centres and Hospitals were presented with an almost impossible task of faithfully recording and documenting all transactions relating to the issue and use of blood and blood products. The Service as a whole, which must draw in the Hospital blood banks, must be held accountable for every unit or component unit of blood which is bled, processed, issued and transfused. The manual mechanisms for dealing with such information are labour intensive, relatively inefficient, difficult to monitor and suspect to transcription error. It was therefore inevitable that many Centres sought to computerise their donor records and provide links to the automated grouping and provision of data handling systems to accommodate effective blood bank inventory and stock control. Most Centres and many hospital blood banks have sophisticated data management systems to facilitate the demands of accountability. Eventually, the facilities for ready access of information on blood stocks may well be linked to hospital inventories to enable the ultimate control and efficiency of blood distribution, use and location.

The dilemma of AIDS with its associated high level of fatality in the U.S.A. re-emphasised an awareness of transmittable diseases, particularly those of viral origin where is some cases no markers had been found to enable adequate screening of donors. Fortunately in respect of the AIDS-related virus, HIV 1, the production of the appropriate antibody, that is anti-HIV 1 in infected subjects, provided a mechanism for screening donors for this transmittable agent. Since September 1985 all RTC's in the U.K. have been screening donors for anti-HIV so excluding the highest risk candidates from the main donor population. Continual improvements have been made in the effectiveness of these tests and the prediction that the future would see the provision of further tests designed to detect other possible viral agents associated with AIDS has been realised by the recent introduction of a test for HIV 2. Furthermore, the recent isolation of a readily identifiable marker correlated with the agents of Non-A Non-B Hepatitis (HCV) will undoubtedly demand large scale routine screening of donors to exclude this transmittable agent.

LOOKING TO THE FUTURE

The pace and level of microbiological screening of donors is likely to continue unabated into the 90's. There is now an increasing demand for cytomegalovirus (CMV) negative blood to support certain immuno compromised patients and it is likely that further tests will be developed for viral agents associated with AIDS, Hepatitis and adult T cell leukaemia, in addition to tests which may be demanded for surrogate markers of Hepatitis, e.g. alanine aminotransferase (ALT) and Anti-HBc.

The increasing demands for extra facilities for further transplant surgery, in particular bone marrow transplants, will compel expansion in the support services provided by the Transfusion Service. The development of selected panels of donors of specific tissue types for support of prospective transplant candidates with HLA antibodies must be accelerated and, once again, the need for some level of

computerisation has already been recognised and rapid developments can be anticipated in this field of work.

These are challenges enough but in addition two further developments of the 80's are threatening to rock the foundations of the Service in the future. One of these is driven by legal considerations and relates to the development of quality assurance programmes and the other is financially orientated and relates to cross charging now defined as 'budget devolution'.

In the mid-80's it became abundantly clear that there was a requirement for the Service to conform to the strict codes of practice applying to the Pharmaceutical Industry embodied in Good Pharmaceutical Manufacturing Practice (GMP). Quite apart from demands of Health & Safety fortified by the requirements under the new massive regulation appertaining to Control of Substances Hazardous to Health (COSHH) and the introduction of the Data Protection Act, the implementation of the Consumer Protection Act and considerations of Product Liability have now to seriously influence our thinking. It is therefore not too surprising that with regular inspections by the Medicines Inspectorate there has been, and will be in the future, significant developments in quality control and quality assurance procedures within the Centres. Independent quality control sections have emerged demanding their own staff and heads of department who have considerable influence over the release of products. In support of these developments a plethora of guideline documents have emerged many aimed at the hospital service as well as the transfusion service. These documents cover subjects such as Compatibility Testing, Documentation & Procedures, Product Liability and Standard Operating Procedures, Maximum Surgical Blood Ordering Schedules and Hospital Blood Bank Computerisation, but the major guideline document directed at the Blood Transfusion Service in the United Kingdom was published in 1989 and released in 1990 and will have far-reaching consequences in component and reagent production.

Even before the publication of the Government's White Paper 'Working for Patients' the wheels were already in motion to exercise the simulation of cross charging for raw material sent to the Blood Products Laboratory (now Bio-Products Laboratory – BPL) Elstree and in reciprocation, for Centres to pay for the range of products produced centrally e.g. albumin, Factor VIII, etc. This exercise is now being extended to include the charging of blood and blood products to District Hospitals based on the fact that the hospital will receive a budget devolved from the Region. It is claimed that this development will create a much more efficient service, will prevent the abuse in the use of blood products and will generate effective economies in the Service but this remains to be seen. One factor must be emphasized and is paramount in all these considerations and that is there will never be any charge for the freely donated blood or plasma which is provided by voluntary unpaid donors. All the 'prices', 'charges' and 'costs' referred to in budget devolution relate only to the operational costs involved in collecting, testing, processing and distributing blood and blood products. It is expected that by 1991 these strategies will be operational in all Regions.

It was, in part, anticipated that these immense changes which are accompanying the Service in the future demanded some form of co-ordination and as a consequence a National Directorate was established in October 1988. Thus, while Regional Directors have responsibility for the Centres, the Directorate headed by a National Director was responsible for co-ordinating BTS management and so far, the role has been to balance and maintain National blood supplies and to establish the infra-structure and mechanism to facilitate logical budget devolution and in particular to mount a system of National audits to monitor and compel the provision of a quality service in the future. The extension of these developments in the future will depend on a number of factors not the least of which will be the ability to establish an equitable arrangement between Regional and National requirements.

For those interested in transfusion technology the depth and variety of interest has never been greater, and the knowledge and skill required to accommodate to the rapid changes in the field of blood transfusion must be commensurate with these developments. Initially, students must acquire a firm grasp of basic principles and methodology otherwise no adequate judgements can be made of new technologies or developments.

With the existence of extensive legislative requirements and numerous guidelines it is being increasingly difficult to maintain a control of developments and training on the job will be of paramount importance in the future. There is likely to be a future requirement to measure the competence of health care workers according to nationally accepted procedures and criteria and there will be an increasing pressure to provide more formalised documented training of operatives working in the field of Blood Transfusion. The establishment of structural training regimes will facilitate accreditation in the future and although these are presently being developed for the training MLA's they will undoubtedly be used for the benefit of a wide range of staff in the future.

Blood transfusion technology has long since departed from its subordinate role as an appendage of haematology; it is a science in its own right. The recent formation of 'The British Blood Transfusion Society' embodies this philosophy and provides a focal point for the development of the Transfusion Service in the future which, hopefully, will encompass medical and scientific personnel in Hospital Blood Banks as well as Transfusion Centres.