# INTERNATIONAL BLOOD GROUP REFERENCE LABORATORY (IBGRL)

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## BACKGROUND

When it was established in 1946 the Blood Group Reference Laboratory was administered by the Ministry of Health and was housed in the Lister Institute in Chelsea. Its two main functions were to provide a centralised service for the production of blood grouping reagents and to provide a red cell reference service to the newly formed National Blood Transfusion Service. It was also a centre for the training of doctors and scientists, from the UK and abroad, in blood grouping methodology. During the early years the emphasis for research was on the discovery of new blood groups and their distribution and development of new test methods for blood grouping. In 1945 the BGRL's first director, Dr Arthur Mourant, had collaborated with R.R.A. Coombs and R.R. Race in the development of the antiglobulin test, which is still as important in blood transfusion today as it was 50 years ago. In 1953 the BGRL gained WHO recognition for its red cell reference work and became the IBGRL. The pioneering work for the organisation and compilation of the National and International Panels of Rare Blood Donors was carried out in the early to mid 60's and the first panels were issued in 1968. Many changes have taken place over the years including cessation of reagent production and expansion of reference services and research activities. This article will give a brief account of the laboratory's past and current activities.

Reagent production initially consisted of anti-A, -B, -A,B and -D from human donors although preparations were already underway to supply rarer sera such as anti-M and -N and AHG which were made in immunised rabbits. Over the years, as new blood groups were discovered, the list of specificities grew. By 1983 human based ABO reagents had been superseded by monoclonal reagents followed by anti-D two years later. In 1986 the IBGRL ceased to be involved in blood group reagent production, except in a research and development capacity; routine production was taken over by BPL Diagnostics. IBGRL currently produces a wide range of monoclonal antibodies of different specificities for use in immuno-haematological research.

#### REFERENCE

#### Red Cell Serology

The red cell reference department investigates complex and difficult red cell antigen/antibody problems and many blood group antigens have been discovered through work carried out in this department. During the 50 years of its existence a unique collection of several thousand rare typing sera and over 2,000 rare red cells has been amassed, thus enabling the most complex of problems to be solved. Referrals are received from reference laboratories and specialist blood transfusion laboratories worldwide in addition to those from the UK NBS Centres. They are mainly from patients whose serum reacts with the majority or all red cells tested and compatible donor blood is difficult or impossible to find. Investigations are also undertaken on unusual, rare or novel phenotypes on the red cells of patients and donors - some of which may eventually be registered for the National or International Rare Donor Panels or provide rare cells for exchange schemes. In recent years immunological, biochemical and

molecular biology techniques have added to the serological repertoire. These methods may be used to predict the clinical significance of rarely encountered antibodies and to elucidate the structure of a new and established blood group antigen. This department organises and maintains the Rare Donor Panels which continue to be widely used both nationally and internationally.

## Granulocyte Serology

The IBGRL has over 15 years' experience in granulocyte immunology and has provided a clinical reference service since 1987. The laboratory is pre-eminent in the UK in providing the most comprehensive range of techniques for the detection and identification of granulocyte antibodies on a routine basis. The service uses rare typing sera together with over 400 donors typed for major granulocyte antigens. These donors are also HLA typed and are often HPA typed, thus providing a valuable resource in those cases where granulocyte antigen matched blood products may be required. NA1 and NA2 genotyping is carried out using a PCR based technique.

## Platelet Serology

The IBGRL has almost 20 years' experience in platelet immunology and has provided a clinical reference service since 1987. The service uses a substantial collection of rare typing sera together and a panel of over 500 fully-typed platelet donors. In 1996, results from the ISBT Platelet Serology Workshop confirmed the quality of IBGRL's 'state-of-the-art' service. HPAI - 5 genotyping is carried out using a rapid PCR based technique.

## Anti-D Quantitation

An anti-D quantitation service both supports the production of therapeutic anti-D at BPL and undertakes the testing of preparations referred from manufacturers abroad.

# Membrane Biochemistry

In the last few years, a specialist service has been introduced to analyse the biochemical nature of defects in the membranes of red cells from infants with rare haemolysing conditions. This service uses electrophoretic separation techniques to detect inherited deficiencies in various membrane components and a controlled proteolytic digestion technique to detect variant forms of membrane spectrin.

# Functional analyses of red cell antibodies

The chemiluminescence test (CLT), first developed as a means of measuring granulocyte antibodies, has been used as a reference service since 1992 to assess the clinical significance of red cell antibodies. The CLT predicts the severity of HDN due to anti-D with greater accuracy than antibody quantitation by Autoanalyser. Recent results suggest that the CLT may also predict the clinical significance of antibodies in transfusion cases.

# Fetal Blood Typing

Most recently, in 1995, IBGRL introduced a new service for establishing fetal blood groups by use of molecular genetic methods to analyse DNA from amniocytes present in amniotic fluid. In this way, fetuses at risk from haemolytic disease of the newborn may be identified without exposing them to the additional risks associated with fetal blood sampling. IBGRL's long experience in molecular genetics has enabled it to provide for the NBS a uniquely comprehensive service which is currently being used by several European as well as the majority of English Centres.

## RESEARCH

From the outset to the present day research has been carried out on novel blood group antigens and antibodies. In the 1940's and 1950's additional research was undertaken on the use of proteolytic enzymes in serology and the use of glycerol citrate to freeze red cells. The early 1960's saw the investigation of the role of platelet and leukocyte antibodies in thrombocytopenia and leucopenia and also research into AHG reagents. During the 1980's IBGRL worked closely with BPL Diagnostics in the development and successful launch of ABC and D typing and AHG reagents formulated from products of hybridoma cell lines generated 'in house'. Also during the 1980's and early 1990's immunochemistry and molecular genetics became areas of research for IBGRL. Many significant findings have been made - not least cloning of the Rh, Lu and LW genes and characterisation and expression of the proteins.

In 1995 the NBA approved a proposal to establish a centre of excellence for research in the Transfusion Sciences at Bristol - known as the Bristol Institute for Transfusion Sciences (BITS). BITS brings together research and teaching at the IBGRL and the NBS - Bristol Centre with that in the University of Bristol. BITS is a joint venture between the NBA and University of Bristol and the Institute is recognised as an affiliated Institute of the University.

Current research activities come into three broad categories of *Haemopoesis*, Immunology and Clinical Transfusion. Haemopoesis research incorporates purification and characterisation of haemopoietic progenitor cells, retroviral gene transfer as a basis for gene therapy, the study of cell adhesion molecules, and prenatal blood group determination. Immunology research incorporates diagnostic reagent production and methodology, development of human monoclonal antibodies, use of recombinant DNA techniques to develop novel therapeutic antibodies and genetic engineering of a component to allow the secretion of human IgG. Clinical Transfusion research is that which supports and arises from the reference services. This includes projects aimed at better understanding of the processes involved in the immune destruction of blood cells and development of cellular assays which reflect these processes into clinically useful diagnostic tests. Investigations into the occurrence and pathogenesis of various immune cytopenias and transfusion reactions are being undertaken in the Platelet and Granulocyte Serology department. The Membrane Biochemistry department is investigating the nature of rare membrane abnormalities and the processes involved in some forms of non-immune haemolytic anaemia. The Red Cell Reference Department continues to carry out research on novel blood group antigens and antibodies which, as well as providing important data, also supports and enhances the quality of the reference service and supports other research within the organisation.

#### 1996

After an interim move to Oxford (1982 - 1989) the IBGRL is now sited in Bristol and administered by the NBA. It is obvious from this article that the staff are involved in the provision of a wide range of specialist services. These activities have encouraged research both to develop a series of 'state of the art' services and to exploit the rare and informative samples which tend to be referred. 'Pure' research in Transfusion Science has expanded enormously over the past years and BITS is recognised as an R&D centre of excellence. In conclusion, IBGRL offers a comprehensive reference service both nationally to the NBS and internationally. It also undertakes research and development work in many blood transfusion related areas and can provide specialist advice in these areas.