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History of the West of Scotland Haemophilia Centre, Glasgow, 1950–2019

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History & Humanities

Abstract

Over 70 years, the West of Scotland Haemophilia Centre in the UK has played a leading role in research, education and training. Its staff studied the natural history of haemophilias, their complications, and their treatment complications, pioneered the use of fibrinolytic inhibitors to reduce the risk of receiving a blood transfusion and developed national audit. Collaborations across Scotland with other haemophilia centres and the Scottish National Blood Transfusion Service progressed self-sufficiency in NHS-produced factor concentrates, heat treatments to prevent HIV and hepatitis transmission, and finally, replacement of human by recombinant factor concentrates.

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Introduction

Haemophilias are genetic bleeding disorders due to deficiency of circulating blood coagulation factors. Haemophilia A (factor VIII deficiency) is an X-linked recessive condition of variable severity, with a worldwide prevalence of 1 in 10,000 males, transmitted by female carriers. The understanding of haemophilia[1] was advanced in the 1930s by the discovery that the defective clotting could be corrected by transfusing a plasma fraction, later named antihaemophilic globulin, then factor VIII. This fraction also corrected the defect in a commoner (1 in 1,000), but milder genetic bleeding disorder: von Willebrand's disease (VWD), whose inheritance is usually autosomal dominant and which affects males and females equally. VWD is due to deficiency of von Willebrand factor (VWF), the carrier protein for factor VIII. Haemophilia B (factor IX deficiency, Christmas disease) is clinically similar to haemophilia B, but about six times less common. Other clotting factor deficiencies are rarer.

Following the development of blood transfusion in the 1940s, infusions of plasma were used worldwide to treat bleeding in patients with haemophilias A and B and VWD. In the UK and other countries, regional specialist haemophilia centres were established from the 1950s for diagnosis and registration of patients with bleeding disorders, education of patients, families and healthcare professionals, and provision of timely treatment or prevention of bleeding episodes.[1] We describe the development of the West of Scotland Haemophilia and Thrombosis Centre which achieved a national and international reputation for research, practice and education. In this review we focus on haemophilias; the Centre's contributions in thrombosis will be reviewed elsewhere.

1950–1959

The Glasgow Royal Infirmary (GRI) Haemophilia and Thrombosis Centre was a collaboration between the National Health Service in Scotland and the University of Glasgow. Leslie Davis, appointed to the University's Muirhead Chair of Medicine at GRI in 1945, specialised in haematology. Stuart Douglas, Registrar 1949–1951, obtained a Medical Research Council Research Fellowship at its Blood Coagulation Research Unit in Oxford, with Glyn Macfarlane and Rosemary Biggs. Using a new blood test – the thromboplastin generation test – they differentiated Christmas disease (haemophilia B) from haemophilia A and published their findings in the Christmas edition of the *British Medical Journal* in 1952.[2] Douglas returned to Glasgow in 1953 as Lecturer, then Senior Lecturer and Reader.

During the 1950s, Douglas and Davis developed the West of Scotland Haemophilia Reference Centre as the regional clinical and diagnostic centre. Covering the western half of Scotland, it served the largest area of the UK regional haemophilia centres, and one of its largest populations (over 2.5 million). Douglas (Figure 1) studied suspected cases and their families, referred by local practitioners, established the type and severity of the disorder, registered them at the centre, issued haemophilia cards with the centre's contact details, and educated patients, families and local practitioners about the prevention and management of bleeding.

Patients could attend their local hospital and be managed by a physician with an interest in haematology, and the local blood transfusion service, who could order plasma from the Glasgow and West of Scotland branch of the Scottish National Blood Transfusion Service (SNBTS), with advice as

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Figure 1 Stuart Douglas, founder of the West of Scotland Haemophilia Centre

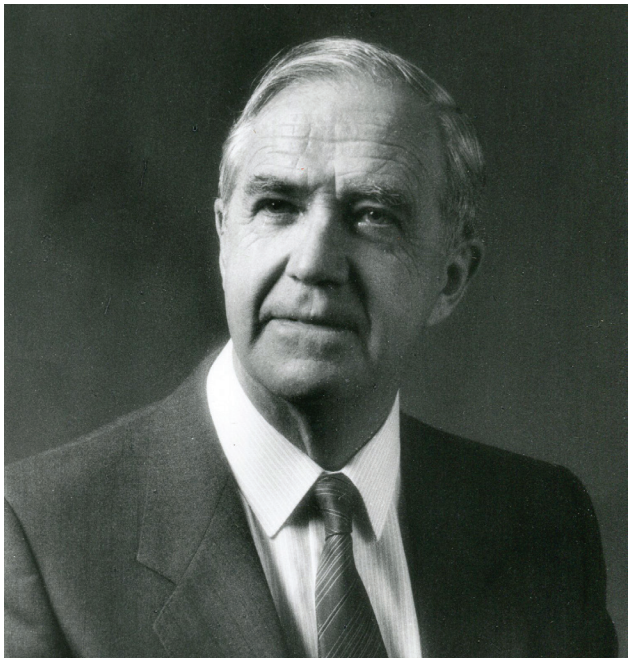


Figure 2 Haemophilic arthritis, 1970s

required from the Reference Centre. Alternatively, patients could self-refer and attend the Centre, where advice and treatment was available at all times. Patients were seen at the Department of Medicine's Wards 2 and 3 on the first floor of the Royal Infirmary, conveniently close to the hospital entrance and casualty department. Children in the Glasgow area were usually treated at the Royal Hospital for Sick Children (RHSC), Glasgow.

The classical feature of haemophilias was excessive bleeding after minor trauma into joints (haemarthrosis), which often led to chronic arthritis (Figure 2), and muscles (which could cause nerve compression). Prolonged treatment with plasma and bed rest, followed by physiotherapy, was often required. Prolonged bleeding after trauma or surgery, even minor surgery such as tooth extraction, was a major and sometimes fatal problem for patients with haemophilia of all severities. Dental extraction for teeth and gum decay was routine in the 1950s. Douglas and his colleague John Orr reported their experience and recommended limiting extractions to two teeth at a time, use of splints and sealants, transfusion of plasma immediately before extraction, and again if bleeding occurred, and antibiotic therapy.[3]

The UK Haemophilia Society started in 1954 and played a vital role in the education and support of patients and families. The Centre encouraged its patients and families to join and to attend meetings of the Scottish branch.

1960–1969

During the 1960s, haematology developed as a clinical and laboratory specialty, and George McDonald was appointed Consultant in 1962. Thereafter the Haematology and Thrombosis Centre had two Co-Directors: Douglas (in charge of the University department's wards where patients were reviewed and treated, and of its coagulation research laboratory), and McDonald (in charge of the NHS routine haematology laboratory and blood bank). They trained their successors Colin Prentice, Charles Forbes, John Davidson and Isobel Walker. At RHSC, Michael Willoughby was appointed Consultant Haematologist in 1963.

The University awarded Douglas a personal professorship in 1964. He was joined by George McNicol, Senior Lecturer. They had an interest in fibrinolysis – the process by which fibrin blood clots dissolve. Since the start of transfusion, blood and plasma were known to potentially transmit viral hepatitis, and patients requiring repeated transfusions were at increased risk. At the Haemophilia Centre, patients and staff were informed of the risks, liver function tests were performed routinely, and episodes of hepatitis reported to SNBTS for donor investigation.

To reduce this risk, McNicol, McDonald and Douglas sought to reduce the amount of blood products used. They pioneered randomised clinical trials of fibrinolytic inhibitor drugs in prevention of bleeding in patients with haemophilia. While ineffective in joint and muscle bleeding, tranexamic acid was effective in minimising plasma use and hepatitis risk after dental extraction and other types of minor surgery,[4] and was subsequently recommended in guidelines.

In patients without haemophilia, the Centre later reported that activated fibrinolysis was associated with adverse outcome after acute gastrointestinal bleeding, and recommended trials of tranexamic acid.[5] Subsequent trials showed that this drug reduced mortality in such patients and reduced bleeding and mortality in patients with major trauma or in childbirth. Use of tranexamic acid has therefore reduced transfusion requirements worldwide.

In 1965 Pool and Shannon in the USA reported that freezing and thawing of fresh plasma produced cryoprecipitate – the first Factor VIII and VWF concentrate, and a more effective treatment of haemophilia and VWD. The GRI Centre reported their experience and its advantages and disadvantages, one of which was that viral hepatitis could still occur.[6]

The UK Haemophilia Centre Directors Organisation (UKHCDO) was established in 1968, recognising regional haemophilia centres, including GRI for the west of Scotland and Edinburgh Royal Infirmary for the east of Scotland.

1970-79

From 1970, a staff nurse and senior house officer in haemophilia were based in the GRI Centre during normal working hours, to deal with enquiries and arrange treatment. Douglas moved to Aberdeen in 1970 and McNicol to Leeds in 1971. They were succeeded by senior lecturers Colin Prentice (Co-Director) and Charles Forbes. In the haematology department John Davidson was appointed Consultant in charge of the Blood Transfusion and Products laboratory, ordering treatments from SNBTS or commercial manufacturers.[7] Isobel Walker was appointed Consultant in 1978, with a remit for perinatal haematology at Glasgow Royal Maternity Hospital and GRI.

Comprehensive care haemophilia centres were developing, including specialist medical and nursing staff liaising with a team of relevant hospital and social work colleagues. In GRI close liaison continued with the dental service. Renal complications (haematuria and ureteric obstruction) were common, reflecting the importance of fibrin to urinary tract integrity[8] and were managed with renal physicians and urologists. Gastrointestinal bleeding was also common[9] and was managed with the department of surgery and gastroenterologists. Haemarthroses and intramuscular bleeds were managed with physiotherapists, rheumatologists and orthopaedic surgeons. Social and psychological issues were studied by Forbes with Professor Ivanna Markova of the Department of Psychology, University of Stirling.[10] These included family issues, education, sport, control of pain from haemarthroses and arthritis, and unemployment. The Centre social worker linked to community services.

Identification of female carriers of haemophilia was important for genetic counselling. Prior to identification of genetic mutations, Prentice and Forbes measured plasma factor VIII antigen and activity in normal and known carrier populations, and calculated predictive odds to inform counselling.[11] They also reported high premature mortality in haemophilia, despite treatment with plasma and cryoprecipitate.[12]

Hepatitis B (HBV) came to public attention in 1970, due to an outbreak in Edinburgh. At haemophilia centres, patients and staff were regularly tested for HBV, in addition to hepatitis risk warnings and Dangerous Specimen labelling of blood samples. HBV testing of blood donors from 1969 reduced the risk of transmission, although there remained a significant infection rate in patients who received SNBTS products.[13] Vaccination was introduced in 1985, and recommended to all healthcare workers at risk, including Haemophilia Centre staff and to Centre patients who were not naturally immune. By 1996 the prevalence of HBV surface antigen positivity in haemophiliacs in developed countries was less than 3%.

Freeze-dried clotting factor concentrates of factors VIII, and IX, were developed in the early 1970s at the SNBTS Protein Fractionation Centre in Edinburgh and by commercial manufacturers. Their advantages over cryoprecipitate and fresh frozen plasma were: assay of factor content resulting in a predictable dose, stability for refrigerator storage, injectability by syringe in a small volume, and few allergic reactions. Concentrates were therefore much more suitable for treatment of major bleeds, trauma and surgery, and for self-administration and home treatment.[14] Disadvantages were: a higher number of plasma donors per batch of concentrate, hence a potentially higher risk of hepatitis, and cost. Forbes and Prentice calculated that provision of home treatment to the 20% of patients who used 80% of the treatment (for frequent bleeds, usually into joints) would cost only 16% more, improve quality of life, enable return to work, and reduce chronic arthritis and hence longterm care costs.[14]

The GRI Centre used concentrates initially for major surgery and major bleeds,[15,16] including the use of prothrombin complex concentrate.[15] For patients with factor VIII inhibitors, which rendered factor VIII concentrates ineffective, porcine factor VIII was used. In RHSC Glasgow, Willoughby, who reviewed home treatment in his textbook of 1977,[17] introduced home treatment for children with severe haemophilia who had frequent bleeds, especially those distant from Glasgow. He reported in 1983 that this had led to a marked reduction in delayed treatment and improved quality of life. To monitor, plan and coordinate increasing use and NHS costs of concentrates, as well as safety issues, annual meetings of SNBTS, the Scottish Home and Health Department (SHHD) and Haemophilia Directors in Scotland were held from 1979, with more frequent meetings of its Coagulation Factor Working Party Subcommittee.

In 1974, John Cash (SNBTS Director) reported that intravenous infusion of the synthetic vasopressin analogue desmopressin raised blood levels of the factor VIII: von Willebrand factor complex, by releasing VWF from vascular endothelium.[18] Such elevations were later shown to be sufficient to treat minor bleeding and to prevent bleeding following dental extractions or other minor surgery in patients with mild haemophilia A or VWD, reducing the use of blood products and the risk of viral hepatitis. After commercial manufacture, it was adopted from 1977 by the GRI Centre, who reported as a side effect symptomatic cerebral oedema from hypo-osmolality due to the drug's antidiuretic effect.[19]

1980-89

During the 1980 Annual General Meeting of UK Haemophilia Centre, Directors at the Royal College of Physicians and Surgeons of Glasgow, Forbes and Prentice organised its first scientific open meeting. International speakers highlighted growing areas of haemophilia care and research, including increasing awareness of non-A non-B hepatitis.

The GRI Haemophilia Centre expanded from two to four rooms, allowing increases in patient waiting, assessment

Figure 3 Home treatment training, 1980s

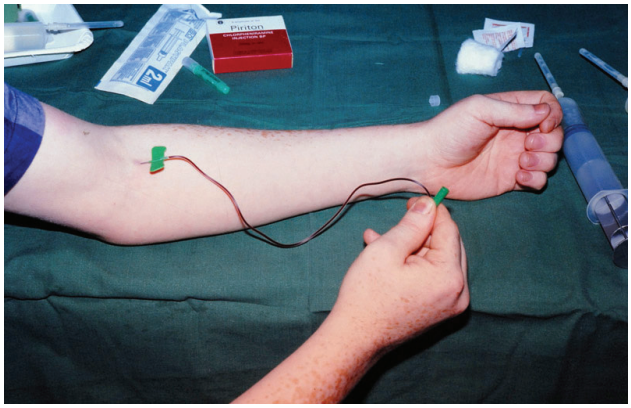
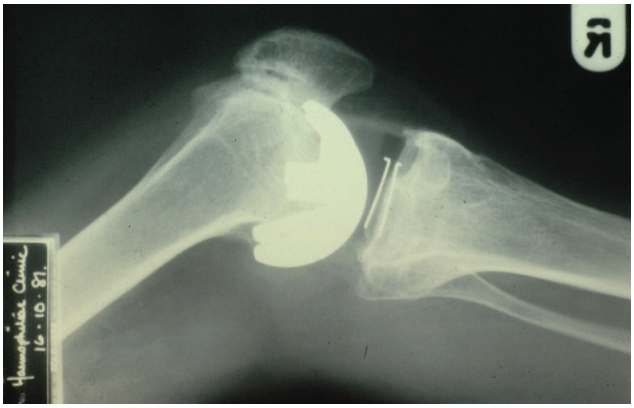


Figure 4 Knee joint replacement surgery, 1980s



and treatment areas. A haemophilia sister was appointed and trained patients for home treatment (Figure 3). A review of 23 adults and 20 children at the GRI and RHSC Haemophilia Centres reported that the ability to treat themselves was perceived by patients as a great improvement.[20]

While home treatment reduced the frequency of musculoskeletal bleeds, many patients remained crippled by chronic arthritis, especially of the knees, for which the only effective treatment was joint replacement surgery, made feasible by use of concentrates. Total knee replacement was performed in five patients with frequent bleeds, severe pain and limitation of movement. Review after 24–48 months showed dramatic lessening of pain and maintenance of a satisfactory level of movement. The frequency of haemarthroses diminished markedly, and the requirements for factor concentrate in the years after operation fell substantially. Two patients returned to employment (Figure 4).[21]

The GRI Department of Haematology evaluated two new treatments for patients with acquired inhibitors to factor VIII: purified porcine factor VIII, and plasma exchange.[22] With the GRI Haemophilia Centre, they also evaluated freeze-dried cryoprecipitate in 14 patients with factor VIII deficiency.[23] The product was not progressed as it could not be virally inactivated. By 1984 Scotland approached self-sufficiency in SNBTS-produced factor VIII and factor IX concentrates, whose viral inactivation was being studied.

In 1982 Michael Willoughby moved to Perth, Australia, and was succeeded at RHSC Glasgow by Ian Hann. In 1983, Colin Prentice moved to Leeds, succeeded by Forbes as Co-Director.

By 1983 cases of acquired immune deficiency syndrome (AIDS) in patients with haemophilia, first described in the USA in 1982, had been reported in the UK. Haemophilia centres kept patients informed of this emerging risk, using haemophilia society newsletters. Forbes collaborated with rheumatologist colleagues to investigate immunological function in the GRI Centre's patients with haemophilia, most of whom had received no commercial (USA) factor VIII concentrate for over two years. They were found to have similar immunological abnormalities (reduced ratio of T-helper to T-suppressor lymphocytes) to those who had received concentrate in the USA. Factor VIII concentrates from both the USA and Scotland also inhibited the in vitro lymphocyte response to mitogens in patients and controls. These results were consistent with a direct immunosuppressive effect of factor VIII concentrates.[24]

In 1984 a retrovirus, subsequently named the Human Immunodeficiency Virus (HIV), was suggested as the cause of AIDS. Forbes collaborated with Danish colleagues to study stored sera from patients in the GRI Centre and a Danish Centre to establish whether antibodies to HIV, a measure of exposure, could be found in European patients with haemophilia, and whether these were related to use of locally produced concentrates vs concentrates imported from the USA.[25] Antibody positivity directly correlated with the use of imported concentrate, but not of locally produced concentrate, indicating that European patients with haemophilia were exposed to HIV via some concentrates obtained from USA donors. In a subsequent report on HIV-antibody status in stored serial plasma samples dating back to 1974 from the 12 HIV-positive patients from the Glasgow Centre, seroconversion occurred from 1981 onward, suggesting that the virus was introduced into Scotland at about the same time as the onset of the AIDS epidemic.[26]

While these findings initially suggested relative safety of SNBTS-produced factor VIII concentrates compared to commercial concentrates, the Edinburgh Haemophilia Centre reported to SNBTS in 1984 that a number of patients tested for HIV antibody were positive, and some had received the same single batch of SNBTS factor VIII concentrate. This study was subsequently published.[27] Meetings between SNBTS and Scottish Haemophilia Centre directors in November and December 1984 resulted in a decision to replace SNBTS factor VIII concentrate with heat-treated concentrate from December 1984. In England and Wales, heat treatment of factor VIII was introduced later, in 1985. Heat treatment of SNBTS factor IX concentrate was introduced in October 1985.

In 1985 Forbes (who had been appointed Chairman of the UKHCDO AIDS Group) sent letters to GRI Haemophilia Centre patients who had received blood products, informing them of

these developments, advising that all patients treated with blood products should take precautions to minimise risk of transmission, and advising that at review appointments the risk of AIDS would be discussed, and in due course HIV testing would be performed, once reliable tests had been established at the Regional Virus Laboratory. A Haemophilia Society information and advice booklet, 'AIDS and the Blood' was enclosed. Forbes informed patients who tested positive for HIV of their result, aided by an experienced counsellor. Gordon Lowe was promoted to consultant and joined Forbes and the counsellor in reviewing patients. Parents of children attending the RHSC Haemophilia Centre were informed and counselled.

The Penrose Inquiry[28] established that 60 people with haemophilia were infected with HIV from treatment with any concentrate in Scotland: 12 at GRI, 21 at RHSC Glasgow, 23 in Edinburgh, 3 in Aberdeen, and 1 at a non-specialist centre. Thirty-nine of these were known to have died by the time of the Inquiry (2010–2015). The percentage of people with haemophilia infected in Scotland was lower than the 19.5% for the UK as a whole.[29] This difference may be attributable to the higher proportion of factor concentrates supplied by the NHS in Scotland, compared to the rest of the UK.

Patients who were HIV-positive were managed jointly with infectious diseases consultants. Patients had access to developing AIDS support services, including access to counselling and psychologists. Forbes chaired the Greater Glasgow Health Board Advisory Group on AIDS, which coordinated the AIDS service, including guidance for dentists, surgeons, laboratories and other healthcare and social work professionals. He became UKHCDO Chairman in 1985. To coordinate activities between haemophilia centres across Scotland and Northern Ireland, he and Christopher Ludlam, Director of the Edinburgh Haemophilia Centre, formed and co-chaired meetings of the Scotland and Northern Ireland Haemophilia Centre Directors.

In 1986, following evidence that the degree of heat treatment of SNBTS factor VIII concentrate (68°C for 24 hrs) was insufficient to eliminate transmission of viral hepatitis, SNBTS heat treatment was intensified (80°C for 72 hrs) and available for clinical use from 1987. The Penrose Inquiry noted that '…Scotland appears to have been the first country in the world that was able to supply all of its haemophilia patients with a factor VIII product that did not transmit hepatitis C.'[28]

The GRI and RHSC haemophilia centres reported a detailed clinical, radiological and laboratory assessment of haemophilic arthritis in 139 patients, including those with mildly and moderately severe haemophilia.[30] Haemarthrosis had affected 70% of patients, including many with mild or moderate disease. 42% had definite and another 15% possible haemophilic arthritis; definite arthritis was seen in some patients with mild haemophilia.

Charles Forbes moved to Dundee at the end of 1987 and was succeeded as Co-Director by Gordon Lowe. Ian Hann moved to London in 1988 and was succeeded by Brenda Gibson. Gibson and Lowe organised regular joint meetings of the children's and adult centres, including planning of transition between centres. McDonald and Lowe were involved in preparation of the first UKHCDO evidence-based treatment guideline issued in 1988. UKHCDO also initiated routine reporting of adverse events of treatments, including infections, inhibitors, and thrombotic events.

To manage the increased workload of the GRI Centre, a staff grade nurse was appointed. The grant-funded Centre counsellor was replaced by a senior social worker for support and counselling of patients and families.

1990–99

George McDonald retired in 1990 and was succeeded as Co-Director by Isobel Walker, and as Head of the Department of Haematology by John Davidson. When Davidson retired in 1996, Walker became Head of the Department of Haematology at GRI, and was President of the British Society of Haematology (1999).

In 1990 Lowe proposed to UKHCDO that national UK clinical audit of haemophilia centres be developed. After a pilot study with Christopher Ludlam, Edinburgh, and Elizabeth Mayne, Belfast, this was initiated across the UK in 1992, with a triennial inspection and report by a haemophilia director from another UK centre.[31] The audit was later expanded to include a haemophilia nurse specialist, and a patient representative from other haemophilia centres.[32] It continues to this day and remains unique for haemophilia.

From 1990 SNBTS developed a programme for manufacture of high-purity factor VIII concentrate. The GRI Centre participated in clinical trials of the concentrate and the product was licensed in 1992.

In 1992 following reports of transmission of hepatitis A from some non-UK factor concentrates, UKHCDO recommended hepatitis A vaccination for patients who were not naturally immune. In the GRI Centre 73 patients were tested for anti-HAV: 40% were positive, comparable with the local prevalence rate for natural immunity. Thirty patients were subsequently treated with SNBTS high-purity factor VIII concentrate: no cases of seroconversion occurred.[33]

Following discovery of the hepatitis C virus (HCV) in 1989 it was established that this was the major cause of non-A, non-B hepatitis. Routine screening of blood donations was introduced throughout the UK in September 1991 using second generation ELISA and RIBA tests. Under 0.1% of UK blood donors were found to be positive for antigen to hepatitis C and were therefore infectious and their donations excluded. This HCV testing was added to routine surveillance for hepatitis in haemophilia centres from 1991 in accordance with UKHCDO discussions and guidance. Patients with positive tests were given information on the virus and its possible effects, and advice on precautions to minimise transmission, testing of sexual partners, minimising

alcohol intake and the need for regular follow-up. This was supplemented with leaflets from the British Liver Trust and/or the UK Haemophilia Society. Further counselling and support was available from the centres' nurses and social workers.

GRI patients with clinical evidence of progressive liver disease were referred to a gastroenterology clinic for further investigation and treatment, including consideration of treatment with interferon or liver transplantation. From 1996 all patients were seen at a weekly haemophilia / hepatitis C clinic by a consultant hepatologist and viral hepatitis nurse specialist sister, and haemophilia nurses. Patients co-infected with HIV were treated by an infectious disease consultant.

By 1993, Scottish and Northern Ireland Haemophilia Centre Directors had completed their previously untreated patient (PUP) study of SNBTS factor VIII or factor IX concentrates, which showed that no patient had developed abnormal liver function tests or antibody to HCV.[34] Patients could therefore be reassured that these products did not transmit hepatitis C.

In 1997 UKHCDO reported an increasing risk of mortality from liver disease and cancer in UK males with haemophilia, due to increasing exposure from the late 1960s, first to cryoprecipitate and then factor concentrates.[35] Over this time period, all-cause mortality in this population decreased steadily.[35] Subsequently, many patients achieved HCV elimination through the development of new effective antiviral therapies. In 2013, haemophilia directors in Scotland reported a follow-up study of 455 patients with bleeding disorders estimated to be infected by coagulation factors provided by NHS Scotland. In 302 with documented HCV infection, rates of natural clearance (17%), genotype frequency (64% genotype 1), and responses to antiviral therapy (15% with monotherapy, 39% with combination therapy) were similar to those in other cohorts. Thirty-four liver biopsies were performed without adverse event, and liver transplantation was performed in 11 patients (7 for liver failure, 4 for hepatocellular carcinoma).[36]

In 1994 the GRI centre was the first to report an association of severe haemophilia A with osteoporosis,[37] which was later confirmed in a meta-analysis.[38]

The Glasgow Centres (GRI and RHSC) were designated Comprehensive Care Haemophilia Centres by UKHCDO in 1993. A secretary and a clinical assistant were appointed. In 1996 John Davidson retired and was succeeded by Campbell Tait, who in 2001 became Co-Director with Lowe and Walker.

At RHSC, a haematology/oncology unit opened in 1996 with dedicated haemophilia facilities. Elizabeth Chalmers was appointed Consultant Haematologist, succeeding Brenda Gibson as Director. Gibson then specialised in haemato-oncology and was awarded an OBE in 2017 for services to this specialty.

In 1996 UKHCDO recommended that recombinant factor VIII concentrate was the treatment of choice for those with

Figure 5 Opening of the new GRI Adult Haemophilia Centre, 1999: left to right: Angus Simpson (Scottish Television presenter), Gordon Lowe, Sister Ishbel McDougall, Isobel Walker, Staff Nurse Elizabeth Little

factor VIII deficiency, being free from human pathogens. The emergence in 1996 of a new variant of Creutzfeldt-Jakob disease (vCJD), identified by the CJD Surveillance Unit in Edinburgh, added to the case for their use. At UK level, information letters were prepared and sent by centres to all patients registered with haemophilia in 2001 and surveillance for vCJD in recipients of blood and plasma products was initiated; no cases have been reported.

As Co-chairs of the Haemophilia Directors of Scotland and Northern Ireland, Lowe and Ludlam met with the Chief Medical Officer for Scotland to request that the NHS in Scotland develop a procedure to replace SNBTS factor concentrates progressively with recombinant concentrates. This was agreed and a consortium established for this purpose. The great majority of patients with haemophilia in Scotland were transferred to recombinant concentrates by 2002, several years before the rest of the UK. Home delivery was commenced in 2007. Operational managers were appointed at haemophilia centres to coordinate product purchase and usage.

After several years of lobbying by the Centre Co-Directors, supported by the local branch of the Haemophilia Society, in October 1999 the GRI Centre moved one floor downstairs to large, modern facilities, occupying the whole of Ward 1 at the hospital entrance (Figure 5).

Lowe was promoted to Professor of Vascular Medicine in 1993 and co-edited a textbook on haemophilia.[31] Walker developed a joint clinic for women with bleeding disorders with the department of obstetrics and gynaecology.[39] Tait developed genetic mutation identification of haemophilia carriers, and genetic counselling, with the University Department of Medical Genetics, and developed transfer of adolescent patients from the RHSC, in joint clinics with Elizabeth Chalmers.

2000–2018

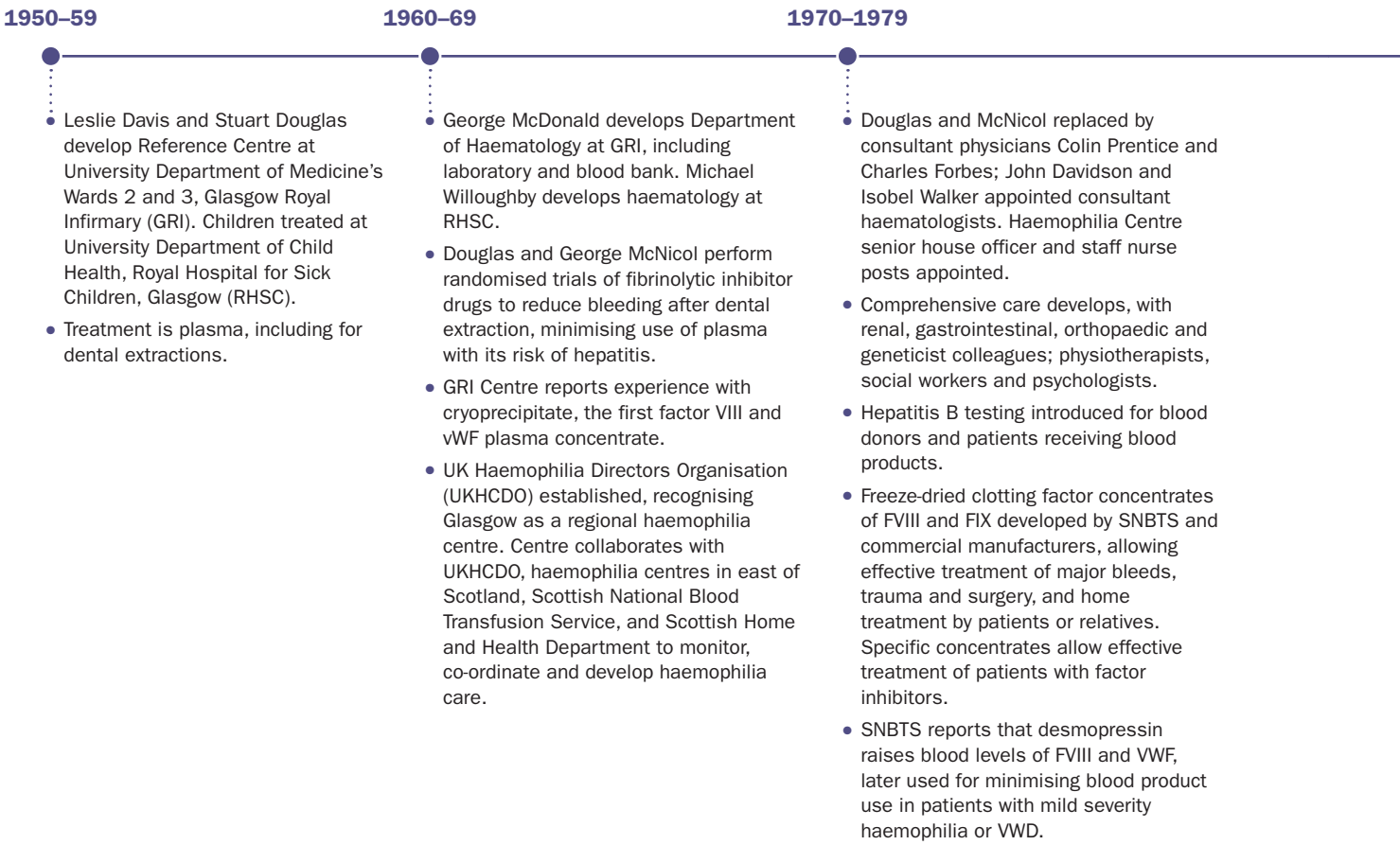
In 2000, to mark 20 years of biannual open scientific meetings of UKHCDO, Walker and Lowe organised the meeting

at the Royal College of Physicians and Surgeons of Glasgow, which had hosted the first one in 1980. Walker was awarded a personal Professorship in Perinatal Haematology by the University in 2003. The clinical assistant was promoted to Associate Specialist in 2005. In 2004 the nursing staff received the annual Health Board nursing award, nominated by Haemophilia Centre patients. They received a further Chairman's Award for nursing in 2017. Walker and Lowe retired in 2009, succeeded as Co-Director by Catherine Bagot, who continued Walker's interest in haemostasis and thrombosis in women, with obstetrician Vicki Brace. A third consultant, Jennifer Travers, was appointed in 2012.

In 2015 the Penrose Inquiry published its Final Report.[28] Its only recommendation was: 'That the Scottish Government takes all reasonable steps to offer an HCV test to everyone in Scotland who has had a blood transfusion before September 1991 and who has not been tested for HCV.'

In 2015 the RHSC Centre moved to the new Haematology/Oncology Unit at the new Royal Hospital for Children. Elizabeth Chalmers chaired the UKHCDO Paediatric Working Party, publishing several reports[40] and was joined by consultant Fernando Pinto.

Figure 6 Timeline for West of Scotland Haemophilia Centre



In the GRI Centre Tait was awarded a personal Professorship in Haemostasis and Thrombosis by the University in 2016. A clinical psychologist began providing psychological services to adult and paediatric haemophilia centres (Glasgow and Edinburgh) from 2016.

The adult and paediatric centres continue to take part in national and international studies of inhibitor development, intracranial bleeding (including neonatal), and clinical trials investigating novel therapies for haemophilias, including gene therapy. The first patient received this at GRI in 2017.

In conclusion: over the 35 years from 1950 to 1984, increasingly effective treatments for patients with haemophilias greatly reduced their painful and disabling bleeding episodes, progressively crippling arthritis, hospital admission rates, and premature mortality from major bleeds. However, over the 35 years from 1985 to 2020, these advances were mitigated by the increasing morbidity and mortality of transfusion-transmitted infections: HIV and hepatitis B and C. In the current century, use of non-human factor concentrates is predicted to maintain low bleeding rates and hence near-normal life quality and expectancy, without further risk of such infections.

Acknowledgements

Figure 1: Source – Royal College of Physicians and Surgeons of Glasgow. Figures 2–5: Source – Medical Illustration Department, Greater Glasgow and Clyde Health Board

1980–89

- Expansion of Haemophilia Centre rooms and staff, including sister at GRI and staff nurse at RHSC, who train patients and relatives for home treatment, which they perceive as a great improvement.
- Successful total knee-joint replacement reported.
- Michael Willoughby replaced by Ian Hann at RHSC.
- AIDS reported in UK patients with haemophilia in 1983. Glasgow and Edinburgh centres report immunological abnormalities in patients receiving factor concentrates. In 1984 HIV antibodies reported in some patients in Scotland who had received commercial or SNBTS concentrates.
- SNBTS introduce heat treatment of SNBTS FVIII concentrate in December 1984, then of FIX concentrate in October 1985. Commercial manufacturers also introduce viral inactivation. Routine HIV-testing of blood donors and patients receiving blood products introduced in 1985. GRI and RHSC appoint HIV counsellors and refer patients to infectious diseases colleagues for joint care.
- SNBTS intensifies heat treatment of FVIII concentrate in 1987. Haemophilia centres across Scotland initiate a prospective study which confirms lack of transmission of hepatitis, hepatitis C or HIV.
- Gordon Lowe replaces Charles Forbes, and Brenda Gibson replaces Ian Hann in 1988.

1990–99

- Routine hepatitis C testing of blood donors and patients receiving blood products introduced in 1991.
- Centre initiates Haemophilia Centre audit, first in Scotland, then across the UK through UKHCDO in 1992.
- SNBTS develops high purity FVIII concentrate, licensed in 1992.
- Centre recognised by UKHCDO as Comprehensive Care Centre in 1993. Walker develops joint clinic with Department of Obstetrics for women with bleeding disorders.
- GRI joint haemophilia/hepatitis C clinic established with gastroenterologist in 1996.
- John Davidson replaced by Campbell Tait, who develops genetic testing and counselling. Brenda Gibson replaced by Elizabeth Chalmers.
- New variant Creutzfeldt-Jacob disease (vCJD) recognised. UKHCDO recommends progressive replacement of human with recombinant factor concentrates.
- New Centre opens in Ward 1 at GRI.

2000–2019

- GRI Centre staff increase with new associate specialist, sister and staff nurses, physiotherapist, secretary and clinical psychologist.
- Walker and Lowe retire, replaced by Catherine Bagot and Jennifer Travers.
- RHSC Centre moves to haematology/oncology unit at new Royal Hospital for Children, 2015. Its new staff include consultant, nurses, dentist and physiotherapist.
- Research continues with novel therapies including gene therapy; first GRI patient treated 2017.

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