

THE
PENROSE
INQUIRY

Final Report

Executive Summary

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under section 26 of the Inquiries Act 2005.

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CONTENTS

	Page
Introduction	1
Genesis of the Inquiry	1
Terms of Reference	2
The work of the Inquiry	2
Patients who were at risk of infection	3
Blood transfusion	3
Bleeding disorders	4
Hepatitis C	5
HIV/AIDS	6
Numbers of patients infected	8
<i>Bleeding disorder patients infected with HCV</i>	8
<i>Transfusion patients infected with HCV</i>	8
<i>Bleeding disorder patients infected with HIV</i>	9
<i>Transfusion patients infected with HIV</i>	9
Individual experiences	9
<i>Specific deaths</i>	9
Victor Tamburrini	10
David Black	10
Eileen O'Hara	11
Alexander Black Laing	12
<i>Written accounts</i>	13
<i>Oral testimonies</i>	14
Blood products	14
<i>Large-pool concentrates</i>	14
<i>Haemophilia therapy 1981 to 1984</i>	16
<i>HIV infections in Scotland</i>	18
Edinburgh	18
Aberdeen	18
Glasgow Royal Infirmary	18
Royal Hospital for Sick Children, Glasgow (Yorkhill)	19
<i>Haemophilia therapy 1985 to 1987</i>	19

Viral inactivation of blood products	20
<i>Up to December 1984</i>	20
<i>After 1984</i>	23
Selection and screening of donors	24
<i>Donor selection: hepatitis</i>	24
<i>Donor selection: AIDS</i>	27
<i>Introduction of screening for HIV</i>	28
<i>Surrogate testing for non-A, non-B Hepatitis</i>	30
<i>Introduction of screening for HCV</i>	32
Information to patients	34
<i>Issues regarding HIV</i>	36
Warning of risks	36
Immunological studies	36
Testing of blood samples for HIV	37
Communication of results	38
<i>Issues regarding HCV</i>	39
Warning of risks	39
Testing of samples; communication of results	41
Transfusion patients	41
Look-back	42
Final comments	43

EXECUTIVE SUMMARY

Introduction

This is a summary of the Final Report of the Inquiry into the transmission of blood-borne viruses to people in Scotland in the course of medical treatment provided by the NHS. The viruses, HIV and Hepatitis C, cause life-threatening illness. Some of those who became ill following infection with one or both of these viruses died as a result, and others continue to live with serious ill-health. Why and how that occurred has been investigated in depth by the Inquiry and the results of that investigation are set out in full in the Report.

This summary presents a brief account of the Inquiry's findings. It also makes reference to procedural matters where necessary, but a full account of the process followed by the Inquiry, as well as its organisation and administration, is contained in the Appendices to the Report. The Appendices also detail those designated as core participants for the purposes of the hearings, and the witnesses who provided evidence to those hearings.

Before turning to the findings of the Inquiry, it is necessary to explain the background to its establishment, its Terms of Reference and the stages in which the Inquiry was conducted.

Genesis of the Inquiry

On 18 April 2006, the Health Committee of the Scottish Parliament called for a public inquiry into the infection of people with Hepatitis C from NHS treatment. The then Scottish Executive decided not to hold an inquiry, but the Scottish National Party made a commitment in its 2007 manifesto to hold such an inquiry if elected to form the government in Scotland.

Separately, the personal representatives of Reverend David Black and Mrs Eileen O'Hara, two individuals who appeared to have acquired Hepatitis C from NHS treatment with blood or blood products in Scotland and who had since died, raised proceedings in the Court of Session to challenge decisions not to conduct investigations into those deaths. The challenges were successful, the court taking the view that under Article 2 of the European Convention on Human Rights, the applicants were entitled to an independent inquiry into the deaths of their relatives.

On 23 April 2008, the Cabinet Secretary for Health and Wellbeing made a statement to the Scottish Parliament, announcing the establishment of the promised Inquiry, which would examine the circumstances in which the infections occurred, up to the introduction of a test for Hepatitis C in donated blood in 1991. The deaths of Reverend Black and Mrs O'Hara would be specifically investigated. The Cabinet Secretary confirmed that the Inquiry would also examine infection with HIV in the course of NHS treatment in Scotland. The Inquiry was to be chaired by Lady Cosgrove but, in September 2008, Lady Cosgrove withdrew for family reasons and Lord Penrose was appointed to succeed her.

At the time of the appointment of Lord Penrose as Chairman in January 2009, the Cabinet Secretary requested that the focus of the investigation be on the period from 1 January 1974, with reference to periods before that date in certain circumstances. The reference period for the Inquiry was therefore almost 18 years (1 January 1974 to 1 September 1991).

Terms of Reference

Terms of Reference for the Inquiry, specifying what was to be investigated, were set out at the time of the appointment of the Chairman at the beginning of 2009, although they were augmented in November 2009 by the addition of the names of another three individuals whose deaths the Inquiry was required to investigate. These Terms of Reference are reproduced in full at the conclusion of this summary. Broadly, in addition to the deaths of named individuals, the Inquiry was required to investigate and report on the following general aspects of the transmission of HIV and Hepatitis C through the use of blood and blood products in NHS treatment in Scotland:

- Collection of blood by donation, and the preparation and supply of blood products.
- Steps taken to prevent the supply of infected blood and blood products to patients.
- Information provided to patients about the risks of infection through treatment.
- Testing of patients for the presence of viral infection.
- Numbers of patients infected with one or both viruses.
- Steps taken to trace patients who had acquired infection.
- Provision of information and treatment to those who had acquired infection.
- The effects of such infection on individuals and their families.

The Inquiry was not specifically required to investigate the death of any individual who had acquired HIV from blood or blood products but, in the course of leading evidence from those who had been personally affected by this tragedy, the deaths from AIDS of three individuals who had acquired HIV from blood products were examined.

Before the oral hearings, the investigation into the death of one of the individuals specifically referred to in the Terms of Reference was discontinued, at the request of his family.

The work of the Inquiry

The work of the Inquiry to fulfil these Terms of Reference has been carried out in four stages: reading of background material and familiarisation with the subject matter of the remit; preparation and publication of a Preliminary Report; public hearings; and preparation and publication of the Final Report.

Appointment of an Inquiry team and the familiarisation of that team with the science of the viruses, the history of blood transfusion and haemophilia therapy, the arrangements for the manufacture of blood products and the supply of blood and blood products by the NHS in Scotland, comprised the first stage of the task. Few aspects of the general story were peculiar to Scotland – the transmission of the Hepatitis C virus (HCV) and HIV by blood and blood products in the course of health care during part of the latter half of the twentieth century, occurred wherever therapy by blood transfusion or administration of blood products was in use. It was therefore necessary for the Inquiry team to consider material from many other countries, particularly England and Wales, other European countries and the USA.

The scope of the Inquiry was very large, since the history of infection in Scotland was long (around 30 years) and the factual material was extensive. The Inquiry therefore concluded

that public hearings would be better conducted against the background of an established narrative of the factual history, rather than taking time during the hearings to establish the basic chronology. The assembly of this narrative and its publication in the form of a Preliminary Report was therefore the second stage of the Inquiry's work. Within the Preliminary Report, the Inquiry published a proposed list of topics for investigation in oral hearings. Those oral hearings were held over 89 days between 8 March 2011 and 30 March 2012, and formed the third stage of the Inquiry. The last stage has been the analysis of the material derived from the three prior stages and the writing of the Final Report, including the sending of warning letters to individuals subject to significant or explicit criticism in draft text. The Final Report is lengthy, running to over 1800 pages. It is organised in five parts. The following paragraphs outline in brief the findings which are set out in full in the Report.

Patients who were at risk of infection

The means by which an individual acquired infection with HIV or HCV (or sometimes both) was by receiving material from blood donated by a donor who carried the virus. In the case of blood transfusion, this occurred directly in the course of a transfusion of donated blood that was required because of illness or injury, or during childbirth or surgery. In the case of haemophilia therapy, it occurred as a result of infusions with blood products, often made from large pools of donations and given to remedy the deficiency of clotting factor in the patient's blood.

The means available to prevent such transmission increased during the period investigated by the Inquiry but, in essence, focused on attempts to exclude donors perceived to have higher risk of carrying viruses, testing of donated blood for each virus or, in the case of blood products, treating the product to kill any virus in it. It was not possible to treat blood itself to kill viruses. Testing for each virus, whether in donated blood or in blood product, was not possible prior to its discovery. HIV was first identified in Paris in 1983, although international acceptance that this was the virus which caused AIDS did not crystallise until 1984. It was not given the name HIV until 1986, but references to the virus in this summary will use that name throughout.

HCV was first identified in the USA in 1988, although details of the discovery were not published until 1989, when the first tests for the virus also became available.

Blood transfusion

Although blood transfusion had been practised in the UK since the nineteenth century, this was on a local basis. A national blood transfusion service for Scotland was established in 1940, and continues to exist as the Scottish National Blood Transfusion Service (SNBTS). In 1974, responsibility for the provision of blood and related services, including production of blood fractions, was delegated by the Secretary of State to the Common Services Agency. During the period investigated by the Inquiry, the Service was organised into five regional transfusion centres, each with a medical director. These were: Glasgow and West of Scotland; Edinburgh and South East Scotland; East of Scotland (based in Dundee); North East Scotland (based in Aberdeen) and North of Scotland (based in Inverness). The Service organised the collection of blood from donors, and distribution of material for transfusion. From the beginning of the 1970s, there was an increase in the transfusion of individual components rather than whole blood, these being red cells, platelets and plasma.

Since the 1950s, blood products have also been manufactured in Scotland. From 1975, this was undertaken by the SNBTS at a purpose-built centre, the Protein Fractionation Centre (PFC), at Liberton in Edinburgh. The PFC manufactured factor concentrates for NHS treatment, using plasma obtained from donations made around Scotland and, subsequently, Northern Ireland also. The concentrates were then distributed around Scotland, and to Northern Ireland, for the treatment of patients with bleeding disorders.

Since at least the 1940s, it had been recognised that blood transfusion could transmit hepatitis, associated with clinical jaundice and then generally known as 'jaundice'. This was assumed to be caused by the transmission in the blood of an agent which caused the disease. The position became clearer as the various hepatitis viruses were discovered.

Bleeding disorders

The bleeding disorders relevant to this Inquiry are Haemophilia A, Haemophilia B and von Willebrand's disease. Haemophilia A is more common than Haemophilia B, and von Willebrand's disease is the most common of the three disorders. All three of these conditions have the characteristic that the blood of an individual is deficient in a particular protein which is necessary for the clotting process to operate. Haemophilia A indicates that the missing protein, or coagulation factor, is Factor VIII. Haemophilia B (also known as Christmas disease) denotes a lack of Factor IX. Von Willebrand's disease indicates a lack of von Willebrand's factor, a protein which binds to Factor VIII and is also involved in the clotting process. All three of these disorders are genetic, although in rare instances can be acquired. Often, the disorder runs through families, but spontaneous genetic mutation can also lead to the condition. Haemophilia affects males, although females who carry the gene can also have reduced levels of clotting factor. Von Willebrand's disease affects both males and females.

Haemophilia is graded as mild, moderate or severe, depending on the level of the relevant factor in the patient's blood. People with haemophilia are at risk of prolonged bleeding; internal bleeding is particularly serious. Bleeding into joints can lead to permanent damage and bleeding into the brain or gut can be fatal. People with severe haemophilia are at risk of spontaneous bleeding. For these reasons, haemophilia, if untreated, can cause major adverse effects on lifestyle and, as a result of recurrent bleeds, serious disability.

In the first half of the twentieth century, treatments for haemophilia consisted of bed rest and, in some instances, transfusion of blood or plasma. The development of technology to separate plasma into its various components improved haemophilia treatment. From the 1950s, in Scotland and elsewhere, early forms of factor concentrates were produced and, from the 1960s, treatment with cryoprecipitate took place. Cryoprecipitate was the solid residue left when frozen plasma was thawed; it was ascertained that this residue contained high levels of Factor VIII and was therefore suitable for treatment of Haemophilia A. Since Factor IX was contained in the liquid portion of the thawed product (the supernatant), cryoprecipitate was not suitable for treatment of Haemophilia B.

In the 1970s, commercially produced factor concentrates, made from large pools of donations, began to be available from the USA, and similar products were manufactured in the UK by NHS facilities – in Scotland, the Protein Fractionation Centre in Edinburgh, referred to above. As NHS products, these were supplied free of charge. Concentrates were very much more convenient to handle, and could be self-administered by patients at home. This led to large numbers of people with haemophilia being able to treat

themselves, and children with haemophilia being injected with concentrates by their parents. For people with severe haemophilia, prophylactic treatment with concentrates also developed, in order to prevent episodes of bleeding. The lifestyle of individuals with haemophilia was greatly improved; the life expectancy of those whose disease was severe was significantly extended.

As with transfusion, however, it was appreciated that hepatitis, or jaundice, could follow treatment with factor concentrates or cryoprecipitate. Such liver disease associated with early concentrate was first reported in 1963 and, associated with cryoprecipitate, first reported in 1969.

Hepatitis C

It is now appreciated that liver disease – hepatitis – can be caused by a number of different viruses. By the mid-1960s, a distinction was being drawn between ‘infective hepatitis’ and ‘serum hepatitis’, the former being acquired by ingestion of the causative agent (enterally) and the latter by transmission of blood or other body fluid (parenterally). Infectious hepatitis became known as type A, and serum hepatitis as type B.

The Hepatitis B virus (HBV), a virus transmissible parenterally, was identified by Blumberg and others in their work between 1963 and 1967. In 1973, discovery of the Hepatitis A virus (HAV), an enterally transmitted virus, was reported by Feinstone and others. The discovery of the viruses led to the development of tests for their presence. In 1972, the UK introduced screening of donated blood for the presence of HBV. At that time, the tests were not sufficiently sensitive to detect all incidences of HBV, and transmission of the virus therefore continued. By 1974, it was also being suggested that many cases of hepatitis in recipients of blood or blood products were not caused by either HAV or HBV. Such cases were attributed to what was termed non-A, non-B Hepatitis (NANB Hepatitis). At that time, it was generally thought to be a relatively mild condition. That understanding was to change, but not until about 10 years later. In the absence of a definitive test, its prevalence was impossible to determine.

Over the period 1975 to 1985, research projects worldwide continued to explore both the prevalence and the seriousness of NANB Hepatitis. Recognition of cases was not uniform, with the diagnosis being made in the USA on the basis of raised liver enzymes without other explanation, whereas in the UK the diagnostic criteria generally applied sought, in addition, other clinical indications of hepatitis. The true extent of liver damage in an individual could not be accurately assessed other than by liver biopsy, a more hazardous procedure in patients with haemophilia. Nevertheless, it became gradually apparent that NANB Hepatitis could lead to chronic persistent hepatitis and chronic active hepatitis (involving more widespread inflammation than persistent hepatitis) and, in a proportion of those with chronic disease, cirrhosis of the liver. By 1985, there was a growing perception that the seriousness of the disease had been underestimated.

Identification of HCV was scientifically challenging. Success was only achieved in 1988, when the Chiron Corporation in the USA announced that they had discovered the virus, although details of the discovery were not published until 1989. It was then recognised that this virus was the cause of most cases of NANB Hepatitis. Tests for the virus were developed and screening of donated blood for HCV was introduced. In the ensuing years, it was ascertained that the virus had six main genotypes, with varying distributions worldwide. The genotype in an individual may influence their response to drug treatment.

Since discovery of the responsible virus, understanding of the natural history of Hepatitis C has progressed. Long-term monitoring of cohorts of patients has also been possible. The virus may cause acute illness at the time of infection, including jaundice; alternatively, there may be no symptoms. A proportion of those infected, 20–40%, will clear the virus naturally within six months, but the rest will develop chronic infection. A proportion of those people will develop cirrhosis; around 1990, it was estimated that this proportion would be about 20%, but the figure is now projected to be higher. Co-infection with HIV worsens the prognosis.

The period within which cirrhosis develops can vary widely: one study in the Midlands found a mean time from infection to cirrhosis of around 30 years. A number of factors are recognised as influencing the likelihood of progression to cirrhosis, including obesity, smoking, alcohol consumption and age at infection. The two principal complications of cirrhosis are oesophageal varices, which cause internal bleeding, and hepatocellular carcinoma.

The effects of chronic Hepatitis C infection can vary widely and may include fatigue, nausea, digestive problems, abdominal pain, itching and flu-like symptoms. Neuropsychological effects, such as depression or cognitive impairment, are also well documented.

Since the early 1990s, treatment for Hepatitis C has involved the use of Interferon, initially singly and then with Ribavirin. The side-effects of treatment with these drugs are severe. Other medications have been and are being developed. Success rates of treatment have increased considerably. For end-stage liver disease, or hepatocellular carcinoma, transplant may be an option, but a patient with Hepatitis C at surgery can expect recurrence of the virus in the new liver.

HIV/AIDS

In 1981 PCP, an unusual and particularly serious form of pneumonia, was reported in five homosexual men in California. The men did not know each other. This report was quickly followed by a report of 26 homosexual men with Kaposi's sarcoma, a rare type of cancer which affects connective tissue. These patients had been discovered to be suffering from impaired immunity, without any history to explain it. Reports of similar disease in other parts of the USA continued over the following months.

In December 1981, *The Lancet* carried a report from London of what appeared to be the same syndrome in a homosexual man who had been a regular traveller to the USA. In the same month, there was also a report of similar symptoms in intravenous drug users in the USA. Initial knowledge of AIDS in the UK existed mainly among infectious diseases physicians. The first report of a case of AIDS in a Scottish patient did not appear until February 1984. The patient was a heterosexual man who had worked in Africa. It is apparent, however, from the report in the *British Medical Journal (BMJ)*, that he had an episode of illness in 1982, although the nature of his condition was not diagnosed at that time.

In July 1982, PCP was reported in three patients with haemophilia, from geographically distant parts of the USA. Reports had also been made of opportunistic infections and cases of Kaposi's sarcoma in people from Haiti living in the USA. In December 1982, there was a report of what appeared to be a case of AIDS in a 20-month-old child in San Francisco who had received a blood transfusion.

In its destruction of the immune system, with consequent development of opportunistic infections and rare tumours, AIDS was a new and unprecedented disease. Initially, it was suspected that there was a connection with a homosexual lifestyle, but the occurrence of the disease in other specific groups pointed away from that hypothesis. Although evidence that AIDS was caused by a blood-borne transmissible agent accumulated in the period 1981 to 1984, there were other theories concerning its aetiology, founded in part on puzzling features such as the absence of physiological appearance of infection and differences in patterns of infection in the various groups affected. Among haemophilia clinicians, there was reluctance to accept that the disease was being transmitted by blood products and a competing theory, that it was due to 'antigen overload' resulting from exposure to material from thousands of donors, gained ground.

As noted above, the HIV virus was first identified in Paris in 1983 (the French discovery was given the name LAV, the name HIV not being introduced until 1986). Discovery of the virus that appeared to be the cause of AIDS (named HTLV-III) was announced in the USA in April 1984, although it was confirmed over a period of years that the American discovery was of the same virus as had been discovered in Paris. After the announcement in the USA in 1984, acceptance that this was indeed the explanation for the disease, including in people with haemophilia, generally followed. Tests for the virus were developed and, in the UK, testing of blood samples from patients to ascertain if they had the virus, began in the summer of 1984. It was ascertained that large numbers of haemophilia patients were HIV-positive, many being asymptomatic at the time of testing. We return to this below.

As is well-known, HIV attacks cells in the immune system, resulting in the eventual erosion of the body's ability to deal with infection or malignant disease. Although HIV antibodies are produced in the human body, these are not able to neutralise the virus. The virus itself is enormously variable. As it replicates, it mutates. It has so far proved impossible to develop a vaccine against it.

At the point when an individual is infected, he or she may experience a short, flu-like illness. At this point, the individual is highly infectious, but there is a lull before antibodies are produced. This is known as the window period, and can be up to three months; tests for the virus which use the antibody as a marker will be negative if undertaken at this time.

A person may remain asymptomatic for some time after infection. Once the immune system has deteriorated, however, and without treatment, the person will develop infection or malignant disease, which will ultimately prove fatal. Other infections (viral, bacterial and fungal) are associated with AIDS, and there can be direct damage to the brain and nervous system.

Throughout the 1980s, people with HIV were unlikely to live more than two or three years after their first AIDS-defining illness. Initially, there was no specific treatment for AIDS; all that could be offered was treatment for whichever AIDS-related condition had developed. In 1986, Zidovudine (AZT) became available for patients with HIV, but studies showed that it had little effect on life expectancy. New drugs became available in the early 1990s and, from 1998, triple therapy, or HAART (highly active antiretroviral treatment) became established. It greatly improved survival. For many, the side-effects of these drugs were major, especially in the early years of therapy.

Full adherence to the treatment regime is important, and patients may require support to maintain this. With such adherence, however, it is likely that the virus in an individual will be fully suppressed.

Numbers of patients infected

It will be apparent that there were four groups of people who were infected in Scotland: patients who acquired HCV from blood product therapy; patients who acquired HCV from blood transfusion; patients who acquired HIV from blood product therapy and patients who acquired HIV from blood transfusion. In the case of people with bleeding disorders, those who acquired HIV were usually infected also with HCV; some people are therefore counted twice. The Inquiry endeavoured to ascertain the number of people in each group. The exercise was difficult. There were sources of data which yielded numbers of transfusion or bleeding disorder patients diagnosed with each virus, sources which relied on total numbers of patients treated with various assumptions as to infection rates, and sources which depended on statistical modelling.

Bleeding disorder patients infected with HCV

The Inquiry was fortunate to have assistance from the Scottish Haemophilia Directors and the UKHCDO (UK Haemophilia Doctors, previously Directors, Organisation). From about 1968, the UKHCDO has collected data on patients with bleeding disorders in the UK, grouped according to the haemophilia centre at which they are registered. Haemophilia centres also retain information about patients. Both bodies carried out analysis of likely numbers of patients infected. Each worked from the assumption that, prior to the achievement in Scotland of successfully heat-treated concentrates (1985 for Haemophilia B and 1987 for Haemophilia A), a patient was likely to have been infected with HCV on their first treatment with concentrates, whether commercial or NHS. Each group further refined its work on the basis of additional information communicated by the other. The Inquiry has accepted the resulting figures.

The estimates finally produced by the Inquiry for bleeding disorder patients infected with HCV are higher than the numbers of cases reported to other bodies. This can be explained by several factors: some patients receiving therapy may not actually have been infected by the virus, a proportion of those infected will have cleared the virus naturally and others with the virus will never have been diagnosed. The Inquiry has reached its conclusion in this area on the basis of the higher figures; these give a figure of 478 people infected with HCV in Scotland as a result of therapy for a bleeding disorder. Some of those people will have died from hepatitis or other causes; as at April 2012, the UKHCDO was aware of 193 patients in this group who had died, 21 of whom had a liver-related cause of death. Of the rest, some may be negative for HCV, some will be living with the symptoms of Hepatitis C, some will have been successfully treated and some may not be aware that they are HCV-positive. The Scottish Haemophilia Directors are attempting to trace any patients in the last category, and the UKHCDO is continuing its work to improve its estimate of the likely total number of patients infected, particularly in relation to those patients treated with blood products other than concentrates.

Transfusion patients infected with HCV

Arriving at an estimate of the number of patients acquiring HCV from blood transfusion took considerable effort on the part of the Inquiry. It is reasonable to assume that the introduction of screening of donated blood for the virus, in September 1991, ended the transmission of HCV by blood transfusion; but it is not possible to determine when such cases first occurred. Until the increase in prevalence of HCV in the general population from around 1970, the number of transfusion-transmitted infections is likely to have been

low. The Inquiry has therefore attempted to estimate the number of people infected with HCV by blood transfusion between 1970 and 1991.

Figures available for people diagnosed with HCV with blood transfusion as the likely cause appeared to the Inquiry to give an unrealistically low estimate of the size of this group. There are several reasons for this, including some of the same factors as operate in relation to bleeding disorder patients, such as natural clearance of the virus or death prior to any diagnosis. In the period under examination, a large proportion of those receiving a blood transfusion died a short time later, in many cases due to their underlying medical condition. Additionally, there is no systematic follow-up of transfusion patients, which reduces the likelihood of identification of HCV, or of attribution of illness to the transfusion.

For these reasons, the Inquiry has based its estimate of the number of people acquiring HCV through blood transfusion in Scotland largely on the results of modelling exercises. These are sensitive to the assumptions on which they are based, but there is no more accurate information available. Taking these exercises into account, the number of people in this group is estimated at 2500.

Bleeding disorder patients infected with HIV

The position in relation to the number of people with bleeding disorders who acquired HIV in Scotland was more straightforward to ascertain. Again, the Inquiry was assisted by both the UKHCDO and the Scottish Haemophilia Directors. These organisations exchanged information and their concluded view was that the number for this group of people was 60, a figure the Inquiry accepts as accurate. Of that number, 23 were infected at the Royal Infirmary of Edinburgh, 12 at the Glasgow Royal Infirmary, three at the Aberdeen Royal Infirmary and 21 at the Royal Hospital for Sick Children in Glasgow (Yorkhill). The final patient was thought to have been infected by treatment at a non-specialist centre.

None of the 59 bleeding disorder patients who acquired HIV at an identified centre had mild haemophilia: in five, the condition was moderate and in 54 severe. Fifty-seven had Haemophilia A and two had Haemophilia B.

On the information available to the Inquiry, 39 of those patients were known to have died.

Transfusion patients infected with HIV

The evidence before the Inquiry indicated that 18 patients were known to have contracted HIV from blood transfusion in Scotland. Ten of these patients were identified through a look-back exercise and eight patients were reported by clinicians as possible cases of transfusion-transmitted infection. Further details about these cases were presented to the Inquiry, and the figure of 18 for this group of people is accepted although, as with cases of HCV from blood transfusion, reliance only on known cases may result in an underestimate. On the information available to the Inquiry, 15 of those 18 people were known to have died.

Individual experiences

Specific deaths

The Inquiry was required to investigate the deaths of four individuals, all of whom were understood to have suffered from Hepatitis C. Evidence was obtained from family members and other factual witnesses, and expert evidence instructed and presented at hearings. The Inquiry's findings in relation to each person are outlined below.

Victor Tamburrini

Mr Tamburrini died on 17 November 2004, at the age of 47, the immediate cause of his death being liver transplant failure and recurrent Hepatitis C.

Mr Tamburrini was diagnosed with Hepatitis C in 2001, at which time he already had severe disease. His condition deteriorated and he underwent liver transplant at the Royal Infirmary of Edinburgh on 26 October 2002. In the summer of 2003, his condition deteriorated and by the end of that year, he had established cirrhosis in the transplanted liver, with recurrent aggressive Hepatitis C. Mr Tamburrini underwent a second liver transplant on 4 February 2004. He did not recover well from this operation, suffering from recurrent Hepatitis C despite antiviral drug therapy. His condition deteriorated and he died on 17 November 2004.

The Inquiry attempted to ascertain how Mr Tamburrini acquired HCV. The first recorded episode of his having surgical treatment was an appendicectomy in 1968. There was nothing to indicate that a blood transfusion was performed in connection with that surgery, and the Inquiry accepted medical evidence that it would be most unlikely. Further hospital treatment was given in 1984, in relation to burns sustained in an accident. Stable Plasma Protein Solution, or SPPS, a blood product containing albumin, was administered. This is a pasteurised product, and there is no record in medical literature of a patient acquiring HCV from such a blood product. In theory, it could occur if the pasteurisation process was defective (as occurred in the USA in 1973, causing Hepatitis B transmission) and the records of the particular batch of SPPS concerned were therefore investigated by the Inquiry, with the assistance of an independent expert on transfusion, Professor Willem van Aken from the Netherlands. No abnormality was found.

In response to suggestions that there might have been a connection with particular facilities and practices criticised by the Medicines Inspectorate after a visit to the PFC in 1981, this scenario was also put to the independent expert. His opinion was that there was no basis for a view that a deficiency in plant or processes at the PFC caused to the issue of any product that may have caused Mr Tamburrini's infection.

Transfusions given to Mr Tamburrini at the time of further surgery in 1998 were also investigated, even though this would be an unlikely occasion of infection, since Mr Tamburrini had had signs of liver disease for some years before 1998. Additionally, he developed liver failure by 2002, which would normally be seen as too soon had infection occurred in 1998. The records pertaining to all the donations transfused to Mr Tamburrini in 1998 were, however, examined and it was established that all donors were HCV-negative.

In these circumstances, the Inquiry concluded that the evidence did not demonstrate that Mr Tamburrini acquired HCV from NHS treatment with blood or blood products and did demonstrate that none of the occasions on which he was known to have received such treatment was the cause of his infection. It is likely that he was infected during the period between his late teens and his early twenties, the cause of that infection being unknown.

David Black

Mr Black died on 31 October 2003, at the age of 66, the immediate cause of his death being hepatocellular carcinoma in a transplanted liver.

Mr Black had suffered from Haemophilia A, graded in his case as mild to moderate. He required occasional treatment for haemorrhage from around the age of five, and

also received therapy in connection with procedures such as tooth extractions. There was limited information available about his treatments in the first few decades of his life, with more detail in medical records from 1960 onwards. In 1965, Mr Black received AHG, an early NHS concentrate, and he is likely also to have received cryoprecipitate in the 1960s. Mr Black was a Baptist minister, and worked abroad, including in the USA where he received haemophilia therapy in 1970, either with cryoprecipitate or with an early large-pool concentrate.

By 1979, Mr Black had developed elevated liver enzymes, a sign of hepatitis infection. It was recognised by 1985 that he had NANB Hepatitis, and in 1987 he was found to have varices, a significant symptom of liver disease. By 1996, his illness had become serious and he underwent liver transplant at the Royal Infirmary of Edinburgh in April of that year. In the years after surgery, Hepatitis C recurred and caused the new liver to develop cirrhosis, which in turn led to the liver cancer from which he died.

It emerged during the Inquiry's investigations that in 1996, Mr Black's own liver, once removed, was discovered in laboratory examination to be cancerous. That information was not communicated to Mr Black, apparently due to an oversight. Had Mr Black been aware of this fact, it is possible that he might have decided to accept antiviral drug therapy after transplant to attempt to prevent recurrence of Hepatitis C in his new liver. It was not possible to determine whether the cancer which developed after the transplant was a recurrence of Mr Black's former cancer or development of the disease anew. On balance, it was probably new disease. That being so, it is possible that earlier drug treatment would have prevented or postponed the development of cancer anew, the size of that possibility being estimated in expert evidence at around 20%.

The Inquiry concluded that Mr Black probably acquired HCV from treatment with blood or blood products by the NHS in the 1960s, that time frame being compatible with the fact that the disease typically takes around 20 years from infection to develop. For Mr Black, with his requirements for haemophilia therapy, infection with HCV was inevitable. There were no reasonable precautions whereby his death could have been prevented and, with the exception of the failure of communication referred to, his medical management was at all times of a high standard.

Eileen O'Hara

Mrs O'Hara died on 7 May 2003, at the age of 72. The immediate cause of her death was acute pancreatitis complicated by sepsis and multi-organ failure. She was also suffering from Hepatitis C, chronic heart failure and type 2 diabetes.

Mrs O'Hara had a complex medical history. It is not possible to resolve with confidence the extent of the contribution made by Hepatitis C to her death, but it can be concluded that she was infected with the virus by blood transfusion.

In 1963, Mrs O'Hara had surgery for a heart condition, and probably underwent transfusion at that time. From her medical records, it was evident that she had transfusions in 1972, 1979 and 1985. Her liver function tests were already abnormal by 1984, and it is most likely that she was infected with HCV by one of the transfusions in the 1970s, more likely the second one, where twice as much blood was given as in the first. Blood for all the transfusions was donated in Scotland; no blood used for transfusion was collected outwith the country.

In 1990, because of her symptoms, Mrs O'Hara was tested for HCV, but the test result was negative. In retrospect, that result was a false negative; it is widely known that the first generation of test kits, one of which was used here, did not detect all cases of the virus. At that time, Mrs O'Hara's heart condition was serious and she required surgical treatment for that. She did not receive care directly related to her liver disease until 1994, when her liver symptoms and their cause were queried by the physician treating her for diabetes. In mid-1995, she was diagnosed as having cirrhosis. Review of her Hepatitis C was sought from a gastroenterologist at Stobhill Hospital. This doctor never actually saw Mrs O'Hara, and issued his opinion on her treatment based on a review of her notes. This deprived her of an opportunity to gain information, and to receive counselling and advice in connection with the illness. The Inquiry concludes that this was a significant lapse in patient management.

Mrs O'Hara experienced serious and increasing symptoms of her liver disease from the middle of 1995 onwards. Her cardiac condition also caused concern, particularly between 1999 and 2002. She became very unwell in March 2003, and underwent surgery, which was not straightforward, for the removal of gallstones. She developed a septic illness and died on 7 May. There were no reasonable precautions which might have been taken to avoid her death.

Alexander Black Laing

Mr Laing died on 4 September 2003 at the age of 79. The immediate cause of his death was liver disease caused by Hepatitis C.

In August 1990, Mr Laing had surgery for bowel cancer. During that surgery, he received a blood transfusion. He made a good recovery from the cancer treatment, but was identified in 1995 through the look-back initiative (explained below) as a person who had received a transfusion of blood from a donor subsequently discovered to be HCV positive. Mr Laing was tested and also discovered to be positive for HCV. Donors who were positive for HCV were generally so due to earlier intravenous drug use or to having themselves received a blood transfusion from an infected donor. In Mr Laing's case, the donor from whom he acquired HCV had received infected blood by transfusion, probably in the 1960s or 1970s. People who receive blood transfusion often proceed to become blood donors themselves. Deferral of donors who had themselves received a blood transfusion was introduced in the UK in 2004, owing to perceived risk from vCJD.

Mr Laing's testing for HCV, and counselling once the result was received, were undertaken by his GP, using nationally agreed guidelines. He was referred to the Aberdeen Royal Infirmary for assessment and care. On assessment, he was considered to be asymptomatic. In 1996, he decided against antiviral drug treatment, a decision which the independent expert instructed by the Inquiry considered to be well-founded, not least because of poor prospects of success. In retrospect, however, Mr Laing probably had established cirrhosis by that point.

Over the period 2000–01, Mr Laing's health deteriorated. He had early liver failure. In June 2003, he became very unwell. He had advanced liver disease, including neurological symptoms, and he died in hospital in September 2003.

In view of his acquisition of HCV from transfusion in 1990, after the virus had been identified, the Inquiry investigated whether the infection could have been prevented had some form of screening of donated blood been in place. It was ascertained that the particular genotype of the virus in Mr Laing's case was genotype 3, a genotype not

successfully detected by the first generation tests for HCV. A sample of blood from the donor had been tested with a first generation test kit, as part of a research project in 1992, and the sample had tested negative for the virus. This demonstrated that, even if HCV screening of donated blood had been in place in the UK in the summer of 1990, HCV in the donation transfused to Mr Laing would not have been detected.

It was also queried whether, had surrogate testing (explained below) been in place, the presence of HCV would have been detected. Based on findings in the research project referred to, the Inquiry concluded that neither testing for elevated levels of ALT nor for the antibody to Hepatitis B core antigen (the markers used in surrogate testing) would have produced an abnormal result with this particular donation.

The Inquiry was not, therefore, able to identify any precautions whereby Mr Laing's death could have been avoided. The view of the independent expert was accepted, to the effect that, once HCV was identified, Mr Laing's management as a patient was an example of exemplary care.

Written accounts

The Inquiry invited anyone affected by the transmission of viral infection by blood or blood products to contact its staff, and many individuals did so. Statements were taken and, excluding those connected to the specific deaths investigated, a total of 159 patients and relatives shared their experiences in this way. Of those, 24 statements concerned the individuals who testified orally, as described below. The written evidence from the other 135 statements is set out in a separate chapter of the Report, and outlined briefly here.

Witnesses spoke of the shock of diagnosis with either HIV or HCV. With HIV, there was horror; the publicity given to AIDS in the 1980s left individuals with little hope on realising their own or their relative's infection. With HCV, there was much less knowledge, causing fear and uncertainty about the future.

Most of those who detailed their experiences had suffered serious symptoms of viral infection, affecting almost every aspect of mental and physical health. Some had also suffered major side-effects from treatment, whether for HIV or HCV. In particular, many witnesses spoke of the significantly debilitating effects of treatment with Interferon, or Interferon with Ribavirin, therapies to treat HCV. Such treatment was not always successful – some individuals had endured three or four unsuccessful courses of therapy. Relatives described watching the suffering of people they loved, including the devastating experience of supporting their children or their partners as they were dying from the effects of infection.

For many, viral infection caused adverse psychological and social effects. Relationships were strained by the consequences of infection. Some who were HIV- or HCV-positive decided to conceal their infection from wider family and friends, causing a sense of isolation and even shame. Others confided in colleagues or friends but did not receive the support they had hoped for. A few were shunned.

Many who narrated their experiences had also suffered financially. Ability to work reduced when symptoms were serious. The opportunity to build up savings or make pension contributions was impaired. Difficulties with insurance were also reported, and much increased expense had been incurred in this and other respects, although most people had also received some financial support from such schemes as have been set up for this purpose.

Not all who contributed to the Inquiry's understanding in this way had experienced a wholly adverse outcome, and a few had been successfully treated for their infection including, in the case of HCV, by liver transplant. But the majority of people had suffered dreadfully and for most of them, life was irremediably altered by viral infection.

Oral testimonies

As well as written statements from many affected by this tragedy, the Inquiry was able to hear personal testimony from those who had lost loved ones and from those who themselves were living with infection acquired through blood or blood products. Family members of people whose deaths were being investigated spoke in person at the hearings, and another seven witnesses testified about the impact of Hepatitis C on them. They included a daughter who had lost her mother to the disease, and two men whose illness had become so severe that they had required to undergo liver transplant. One of these patients also had HIV, but had been more seriously affected by liver disease. The other four were living with the debilitating effects of Hepatitis C, and spoke of the constant impairment of their health and wellbeing. In the summer of 2013, the Inquiry was sad to learn that one of those who gave such evidence had died from liver disease.

Six witnesses affected by the transmission of HIV by blood or blood products spoke of their experience. The Inquiry heard from a mother who had lost her young son, a widow who had lost her husband and a daughter who had lost her father; all three had died of AIDS. A mother whose baby acquired HIV from a blood transfusion at birth told of how her son's life has been affected by the virus, and two men living with HIV spoke of the continuing impact of the condition on them.

There is no summary of the evidence of these witnesses. It is set out in full in the Report, and provides a powerful demonstration of the serious effects of the viruses. Every witness showed great courage in attending to speak of such painful experiences. Many suffered considerable distress in doing so. The Inquiry wishes to pay tribute to them all.

Blood products

The Inquiry examined many different aspects of the manufacture and use of blood products in order to understand how they came to inflict HCV and HIV/AIDS on patients. It was plain that the risks they posed were not always fully understood by all those involved, including the patients.

Large-pool concentrates

As already mentioned, haemophilia treatment in the middle of the twentieth century initially consisted of bed rest and transfusion of blood or plasma, but progressed to involve the administration of blood products. Early forms of Factor VIII concentrate were available in limited quantities in the 1950s; small-scale production was carried out in the Blood Products Unit of the Royal Infirmary of Edinburgh from 1956, with each batch made from around 12 donations. Cryoprecipitate became widely used in the UK from 1966. An NHS Factor IX concentrate, DEFIX, was developed in Edinburgh in 1972.

In 1973, large-pool concentrates made by commercial companies in the USA became available in the UK. These were freeze-dried, and reconstituted at the time of treatment. Concentrates quickly became the product of choice for doctors and patients. Their advantages were that they were more potent and of higher purity than cryoprecipitate, had defined amounts of Factor VIII, and could be filtered to remove bacterial contamination.

Allergic reactions were less common. Concentrates were easier to store and more convenient to use, since cryoprecipitate required to be stored frozen, thawed and then administered, usually in doses of at least 10 to 15 packs for an adult.

For some time, the transmission of hepatitis by treatment for bleeding disorders had been viewed as an alarming side-effect; since 1967, the UKHCDO had been studying transfusion hepatitis. Although it was recognised that large-pool concentrates carried a risk of transmitting hepatitis, it was believed that the risk for patients with severe haemophilia was not much higher than in patients treated with other methods. It was also expected that introduction and refinement of screening of donated blood for Hepatitis B would reduce the problem. Government policy was therefore that factor concentrates should be used, although the UK should attempt to become self-sufficient in the manufacture of these products rather than continue to import them.

In Scotland, the Blood Products Unit at the Royal Infirmary of Edinburgh was renamed the Protein Fractionation Centre, and by 1973, was producing concentrates from batches of 100 litres of plasma. Manufacture of NHS concentrates took place at PFC Liberton from 1975, the plant also producing immunoglobulins, albumin and other products from blood. The manufacturing process as it existed at the end of 1983 was explained in detail to the Inquiry in hearings. By 1983, a batch of product was made from 4000 donations, pooled together; although this was large, the volumes used by commercial companies in the USA were considerably greater, sometimes of the order of 30,000 or more donations.

The methods used by commercial companies in the USA to recruit donors were publicised in the UK in two 'World in Action' documentaries broadcast in December 1975. These programmes were viewed by the Inquiry. Although the practices of recruiting 'skid-row' donors and paying for their donations were perceived at the time as undesirable by British physicians, hepatitis was considered in 1975 to be a diminishing risk, due to the development of screening of blood for Hepatitis B. The cases of hepatitis featured by World in Action were probably Hepatitis B.

The programmes did not effect a change in practice amongst haemophilia clinicians in the UK; on the contrary, the efficacy of factor concentrates led to a burgeoning demand for them, albeit with a general preference for NHS concentrates if possible. The Inquiry pursued the issue of self-sufficiency to ascertain whether Scotland ever achieved this policy goal. The definition of self-sufficiency can differ – it may mean that a country meets its total requirement for factor concentrates from its own production, or it may mean that there is enough domestically produced concentrate to meet the demand for that particular product. In Scotland, use of commercial concentrate never completely ceased during the reference period, even though there appeared to be enough domestically produced material to satisfy total demand. The Inquiry appreciated that there were reasons why commercial concentrate was used in preference to NHS concentrate for some patients at some times; for each patient, individual therapeutic product choices were made by clinicians, as would be expected.

From 1975, use of concentrates in the UK extended to home treatment programmes. Over the next few years, this was accepted as the way forward for haemophilia treatment, with the introduction also of concentrate therapy for prevention of bleeding in some patients with severe haemophilia (prophylaxis). Home treatment was seen as highly efficacious in reducing the morbidity associated with haemophilia, and improving the quality of life for those with the condition; in 1962, the mean age at death of people with severe haemophilia had been 37 and by the early 1980s, life expectancy was near normal.

The risk of hepatitis, now seen as primarily the non-A, non-B form, continued to be recognised: when data were compiled by haemophilia directors in 1976, the practice of monitoring liver function in patients receiving concentrates was already established. The UKHCDO consistently addressed the topic of hepatitis at its meetings, although many haemophilia clinicians perceived this as a risk of jaundice, that is, acute and usually transient illness. At the manufacturing stage, the risk of liver disease from concentrate therapy was also taken into account – research began on possible methods of virus inactivation in the preparation of concentrates, and is outlined further below.

In essence, however, at the beginning of the 1980s, although there had been some medical literature pointing out that concentrates appeared to carry a risk of chronic liver disease, NANB Hepatitis was still considered by haemophilia clinicians to be a mild form of the disease and not to be a contraindication to therapy with concentrates. There was also a perception that commercial concentrates were more likely to cause hepatitis than NHS products, because of the reliance on paid donor recruitment.

The view that a risk/benefit comparison for factor concentrates favoured the continued use of these products was destined to shift in the 1980s, due to the arrival of HIV.

Haemophilia therapy 1981 to 1984

As already mentioned, the first cases of a new syndrome, AIDS, were reported in the USA in June 1981. It was not until the summer of 1982 that a report appeared of similar symptoms in people with haemophilia, also in the USA. The disorder as a whole mystified clinicians, and in the first few years after its emergence, many theories existed about its cause.

In the USA, there was heated debate about the extent of any risk to people with haemophilia. Haemophilia clinicians sought proof that the disease could be caused by blood products, although certain other physicians considered that there was sufficient evidence to justify a review of practice. Recommendations regarding precautionary measures were made in December 1982 by the US National Hemophilia Federation: concentrates should not be introduced to those not previously exposed to them unless there was an overriding medical indication. Examples of those who should not be introduced to concentrates were new-born infants and children under four, newly identified patients and patients with clinically mild haemophilia. A few medical commentators mooted the withdrawal of concentrates, but such suggestions were not accepted; clinicians and patients preferred the status quo of widely available effective treatment to continue.

At this point, there had been only one or two cases of AIDS in the UK, and no cases in people with haemophilia. In the spring of 1983, clinicians in both Glasgow and Edinburgh began research into whether there were immune abnormalities in haemophilia patients treated at their centres. The research demonstrated that there were such abnormalities, but their significance was unclear. The theory that such abnormalities could result from exposure to proteins from many donors continued to persuade some clinicians, and it was also believed that not all those with such abnormalities would become ill and, of those who did, not all would suffer a fatal outcome. In addition, the majority of patients in Scotland were being treated with domestically produced NHS concentrates, and there was considerable confidence in the local blood supply.

In May 1983, in response to particular stories about AIDS in the media, the UK Haemophilia Society issued to members a letter composed by a leading haemophilia clinician. This

letter offered reassurance about the level of any risk posed by AIDS, and asserted that it would be counter-productive to alter treatment programmes radically. That same month, a proposal from the Communicable Diseases Surveillance Centre that import of concentrates from the USA should cease was made to the DHSS. It was considered at a meeting of the Biologicals Sub-committee of the Committee on the Safety of Medicines in July 1983, but rejected due to perception that the degree of risk did not warrant such a course, and to the lack of alternative treatment for people with haemophilia. At that time, most patients in England and Wales were being treated with commercial products imported from the USA.

In June 1983, the Haemophilia Reference Centre Directors issued guidance about treatment, following a meeting in London in May. At that point, there were said to have been 10 cases of AIDS in homosexual males in the UK and one suspected case in a person with haemophilia. DDAVP (a drug which temporarily raised the level of Factor VIII in the blood) should be considered for mildly affected patients with Haemophilia A and von Willebrands disease; policies of reserving NHS concentrate and cryoprecipitate for children, mildly affected patients and patients with no exposure to imported concentrates should continue. It was agreed that there was insufficient evidence to warrant restriction of the use of imported concentrates in other patients, but constant review was required. For Haemophilia B patients, normal supplies of NHS concentrate should continue to be used.

This position was maintained in the autumn of 1983 although, in August, the death had occurred of the first UK haemophilia patient to die of AIDS. A WHO meeting in November 1983 advised against the non-essential use of blood and blood products. In the *BMJ* of December 1983, a leading UK haemophilia clinician expressed the view that the risk of haemorrhage and its complications far outweighed the risk of developing AIDS. At the beginning of 1984, the Haemophilia Society maintained its position that there was no reliable evidence that AIDS was transmitted by blood products, although this still seemed the most popular theory. In its view, more information was required before determining the goal to be pursued in respect of blood products.

As far as government was concerned, the official line which had been used in relation to the question of blood products and AIDS since the summer of 1983 was that there was 'no conclusive evidence' that AIDS was transmitted by blood or blood products. This line was dropped, apparently between January and March 1984. The Inquiry considers the line to have involved a highly nuanced use of language, carrying a risk of misinterpretation. It is noteworthy that in the summer of 1983, there was in preparation a DHSS leaflet for blood donors which said that AIDS was 'almost certainly' transmitted by blood and blood products.

In 1984, the position regarding AIDS and haemophilia changed radically. In the first place, the announcement in the USA in April of the discovery of the causative virus (a similar announcement made the previous year in France had not been generally accepted) ended speculation about other possible causes. Secondly, the discovery of the virus led to the development of tests and the manufacture of test kits. These tests began to be carried out on samples of blood from haemophilia patients in the summer of 1984, and high rates of prevalence in some centres were discovered. Thirdly, at the end of the year, heat treatment effective to destroy the virus was applied to Factor VIII concentrate manufactured in Scotland, and all Factor VIII product distributed by PFC from December 1984 was therefore HIV-safe. Factor IX was not HIV-safe until October 1985.

In its conclusions on this chapter of its investigation, the Inquiry notes that before the general acceptance in 1984 of the aetiology of AIDS and the discovery of its prevalence in people with haemophilia, some clinicians entertained reasonable doubts about both these matters and others, though more pessimistic, saw no opportunity to alter therapy. There was widespread reluctance to abandon known benefit on the basis of suspected risk.

Other than by a general cessation of therapy with concentrates, the infection of haemophilia patients with HIV over the period 1980 to 1984 could not have been prevented. Moreover, the earliest infections in Scotland occurred before 1 January 1981, meaning that any such general cessation would have needed to occur before AIDS itself had been reported. Although advanced by individual clinicians from time to time once AIDS had emerged, the view that concentrate therapy should cease was a minority view, rejected by a large body of informed opinion. After the autumn of 1983, when the first death of a UK haemophilia patient with AIDS had occurred, the Inquiry concludes that it was reasonable to continue to treat patients with concentrates, provided these were used on a more discriminating basis.

HIV infections in Scotland

As previously noted, a total of 60 people with haemophilia were infected with HIV from treatment in Scotland. The rate of infection among haemophilia patients in Scotland, excluding Yorkhill, was 8%. The rate of infection at Yorkhill was 23%.

Edinburgh

As already noted, 23 patients treated at the Royal Infirmary of Edinburgh acquired HIV through haemophilia therapy. Of those, all had Haemophilia A and all had severe deficiency of Factor VIII. All but one were infected by NHS product; the person infected by commercial product appears to have been infected in 1981, before the threat of AIDS to haemophilia patients was known. The preponderance of infection from NHS product is a consequence of a clear treatment policy in Edinburgh from the outset of therapy with large pool concentrates: NHS product was preferred because it was considered safer than imported commercial material. Eighteen of those infected by NHS product form a group of people known as 'the Edinburgh Cohort'; much has been written about this group of patients, who all acquired infection in the period March to May 1984. Investigation has revealed that they appear to have been infected by two or three infected donations, given in the period June to October 1983; it is not possible to determine which part or parts of Scotland were the source of the infected donations. At the time of hearings, all but four of the patients infected in Edinburgh had died.

Aberdeen

Three patients acquired HIV from haemophilia therapy in Aberdeen, all three having Haemophilia A. One patient had moderate haemophilia and the other two were severely affected. Two patients appeared to have been infected by NHS product, one apparently by a batch implicated in the Edinburgh Cohort. The third patient may have been infected by NHS or commercial product. Two of the patients were known to have died by the time of hearings.

Glasgow Royal Infirmary

Twelve patients acquired HIV from haemophilia therapy at the Glasgow Royal Infirmary. Ten had Haemophilia A and two had Haemophilia B. In 10 patients, haemophilia was severe and in two, moderate. Three patients were apparently infected by commercial

product and three by NHS product. The remaining six patients had received treatment with both NHS and commercial product and it was not possible to ascertain which type of product caused their infection. Of the 12 patients, 10 were known to have died by the time of the hearings.

Royal Hospital for Sick Children, Glasgow (Yorkhill)

Twenty-one boys treated at Yorkhill acquired HIV from haemophilia therapy. All had Haemophilia A – two of moderate severity and 19 severe. One patient could be viewed as infected by NHS product, six by either NHS or commercial product and the other 14 by commercial product.

About five boys were infected before the first cases of AIDS in haemophilia patients were reported and up to 16 were infected before the first case of AIDS in a haemophilia patient in the UK. At the time of the hearings, eight were known to have died, the higher survival rate reflecting an apparently better prognosis for those who were young at the time of infection.

The high usage of commercial product at Yorkhill reflected preference on the part of the haemophilia consultant up to the end of 1982. After some research, the Inquiry was able to locate the physician concerned, who had emigrated to Australia at the end of 1982, and explore with him the reasoning behind this policy. Commercial product was considered easier to use in the treatment of children, and this treatment policy was set before AIDS was first reported. From the beginning of 1983, NHS product was used in far greater quantities at Yorkhill, but the majority of infections had occurred by then.

Haemophilia therapy 1985 to 1987

Although a heat-treated Factor VIII concentrate was distributed within Scotland by PFC from December 1984, it was to be more than two years later before a product successfully treated against NANB Hepatitis (Z8) was available from the PFC for people with Haemophilia A. The position was different for Haemophilia B – product heated to a higher temperature, sufficient to destroy HCV, was available from the PFC from October 1985. Research in the early 1980s had revealed that the chance of contracting NANB Hepatitis from concentrates was virtually 100% on first exposure, whether the product was commercial or NHS. This was simply a function of the prevalence of the virus in the donor community, and the size of the pools from which the concentrates were made.

The guidance on treatment issued by the UK Haemophilia Reference Centre Directors in December 1984 was primarily directed towards avoiding the transmission of HIV to patients. But it was emphasised that the products available still posed a risk of transmitting hepatitis. The period 1985 to 1987 was also the time when it became clear that NANB Hepatitis was more serious than had previously been generally appreciated. Treatment decisions in relation to patients with haemophilia were therefore particularly difficult at this time, especially for those who had never previously received concentrate therapy and were therefore presumed free of NANB Hepatitis. If treatment was necessary, both available products posed risk: cryoprecipitate presented a lower risk of hepatitis but posed a risk of HIV, at least until screening of donated blood for HIV was introduced in October 1985. The position with concentrate was the opposite – it was safe against HIV, but almost certain to transmit NANB Hepatitis. Information presented to the Inquiry indicates that at least six previously untreated patients acquired HCV from treatment in Scotland during this period.

In England, the Blood Products Laboratory (BPL) had succeeded in 1985 in producing a Factor VIII concentrate heated to a higher temperature than the then available product in Scotland. This product (8Y), which, from its introduction, was the only NHS Factor VIII product available in England and Wales which was safe against HIV, was later confirmed to be hepatitis safe as well. It was distributed from September 1985.

In May 1986, a patient with mild haemophilia was treated in Edinburgh with Factor VIII concentrate manufactured at the PFC. This process was, however, insufficient to kill the Hepatitis C virus and the patient developed signs of hepatitis shortly after.¹ Within a short time of this occurrence, steps were taken to procure a small supply of 8Y from England, for such an eventuality in future. On 1 August 1986, 50 vials were sent from the BPL; they were kept in Edinburgh and haemophilia clinicians in other parts of Scotland appeared to have had no information that they existed or that it was possible to obtain the material from England.

The Inquiry was also aware of a patient with haemophilia in a remote part of Scotland who received treatment with the heat-treated concentrate manufactured at the PFC during this period and acquired hepatitis.¹

The Inquiry concluded that it was unfortunate that no information about potential use of 8Y in such a situation was disseminated from Edinburgh. There was, however, no basis for a finding that a general supply of the product could have been made available to treat patients in Scotland; demand for NHS heat-treated product in England and Wales exceeded the supply of 8Y. There also appeared to be a lack of provision of guidance to hospitals in Scotland which did not have haemophilia centres, but would be expected to treat a haemophilia patient in an emergency. Within hospitals, there should have been written protocols for junior staff less familiar with the challenges and drawbacks of the forms of therapy available for the treatment of haemophilia at this time.

Viral inactivation of blood products

Up to December 1984

As mentioned earlier, the theoretical possibility of eliminating hepatitis virus or viruses during manufacture of factor concentrates was identified in the 1970s. But it was envisaged as a major challenge – in any process devised the activity of Factor VIII, a heat-sensitive material, would have to be preserved. Further, any additional process would reduce yield, and maximising yield was a priority in an era where national self-sufficiency was the aim and there was high local demand. It was not obvious how all these goals could be met simultaneously.

Initial ideas centred on inactivation by heat, radiation or chemical treatment. Many different attempts had been made using specific techniques in these categories but none had succeeded in eliminating infectivity without unacceptable damage to product. In October 1980, however, it emerged that a German company, Behring, had apparently succeeded in developing a pasteurisation process, using stabilisers to protect the Factor VIII. Full details of how this had been achieved were not disclosed, however, and the yield was reported to be low, at 8%. Nonetheless, the PFC began experiments on pasteurisation of its Factor VIII product, to attempt to replicate the apparent success of Behring. It should be noted that the Behring product was neither licensed nor available in the UK.

¹ Please note that this text has been amended. The first print run of the Executive Summary made reference to 'unheated' Factor VIII rather than to Factor VIII which was heat-treated but not sufficiently to kill the Hepatitis C virus. These events are discussed in more detail in the Final Report in paragraphs 22.54–22.58 of Chapter 22, *Haemophilia Therapy – Use of Blood Products 1985–1987*.

The SNBTS addressed the issue of safety in additional ways, such as by setting up different groups to monitor developments elsewhere and generate ideas. Scientists from the PFC attended international conferences on these topics. Towards the end of 1982, they learned that another commercial company, Hyland, had developed a dry heat-treated Factor VIII product, and intended to promote it as safer than unheated product. Around this time, a decision was taken that the PFC would focus on pasteurisation, in which some promising early steps had been taken.

In general, there was close cooperation between scientists at the PFC and their counterparts in England at the BPL, where research into inactivation of viruses had also begun. The arrival of commercial heat-treated product, and debate about the extent to which it should be tested on patients in the UK, caused tension between the transfusion services in Scotland and England, however, largely due to the difference in reliance on commercial product between the two countries. In the event, the product was subsequently demonstrated to transmit NANB Hepatitis, that being apparent by around the summer of 1983. Insofar as Factor IX was concerned, research on viral inactivation was also taking place by the end of 1982; since there might be added thrombogenicity (potential to cause clots in blood vessels) in the product, it was anticipated that studies would be required on this aspect.

In the spring of 1983, suggestions began to be made that the heat treatment project might require to deal with the causative agent of AIDS. The attempt to produce hepatitis-safe product was essentially directed towards those who had received no or minimal treatment with concentrates, and likely demand for product was assessed on that basis. With a programme directed towards making product HIV-safe, total production would require to be treated, a project of much greater scale. The PFC contemplated accelerating its pasteurisation programme, and application for funding was made to the Scottish Home and Health Department (SHHD), a department within the Scottish Office before devolution. Funding was not finally authorised until August 1984, but the Inquiry was satisfied after investigation that this did not delay progress with the research, the key factors in which were the organisation and conduct of clinical trials.

In England, the BPL decided in 1983 to pursue dry heat treatment. Towards the end of that year, the PFC undertook some experiments with dry heat treatment. Using model viruses (other viruses thought to behave in a similar way to the target virus, necessary where the latter has not been identified) they established that there was less viral kill than with pasteurisation and accordingly, did not change tack. It was anticipated that the distribution of pasteurised product could begin in April 1985.

In the summer of 1984, the PFC was proceeding with this work, and improving the purity of its product in order to reduce the volume of material to be pasteurised. But over the summer, haemophilia clinicians were sending samples from their patients to be tested with the recently devised test for the AIDS virus. At the end of October, it was revealed to the SNBTS that a number of patients treated at the Royal Infirmary of Edinburgh with PFC product between March and May 1984 were positive for the virus – the Edinburgh Cohort, referred to above.

After this news, matters progressed with great speed. Steps were immediately taken to reassess the previous work on dry heat treatment. In November, it was learned informally that the Hyland heat-treated product, although not safe against NANB Hepatitis, appeared not to have transmitted HIV, although published reports to this effect did not appear until February 1985. Scientists from the PFC attended an international conference in the

Netherlands, at which they learned of the success of another commercial company, Cutter, in inactivating the virus by heat treatment at 68°C for one hour. On their return, they immediately implemented a plan to dry heat treat all Factor VIII. A 12-month stock at PFC was heated at 68°C for two hours, and clinical trials were conducted to confirm that the Factor VIII activity was preserved and that the heated product had no adverse side-effects. From the middle of December, a month's supply was distributed to all regional transfusion centres in Scotland, and to Northern Ireland. Unheated product was recalled, including from patients, and replaced with heated product; one or two clinicians were unhappy at the suddenness of the introduction.

In January 1985, the protocol was changed to heating at 68°C for 24 hours, but there is no evidence of HIV transmission by any of the product heated for a shorter time. Initial tests of a heat-treated Factor IX had revealed a problem with thrombogenicity, and collaboration between the PFC and the BPL in England to change the product formulation enabled this to be solved. Animal tests on product heated at 80° for 72 hours were completed satisfactorily in August 1985. Heat-treated PFC Factor IX was issued routinely from October 1985.

Particular aspects of the heat-treatment programme in Scotland were investigated by the Inquiry, in order to ascertain whether a supply of concentrate successfully treated against HIV could have been available earlier than December 1984/October 1985. In this aspect of its work, the Inquiry was again assisted by Professor van Aken.

The Inquiry investigated whether the viral inactivation programme at the PFC in 1983 and 1984 was informed by a sufficiently serious view of the risk of AIDS. It concluded that risk was viewed appropriately. A theoretical possibility that the causative agent would enter the UK blood supply was acknowledged, but there were no data to indicate that this had occurred until tests were conducted over the summer of 1984. With justification, UK blood had been viewed as safer than the plasma used in the manufacture of commercial concentrates in the USA.

Should the PFC have accelerated its heat-treatment programme from the spring of 1983? The Inquiry investigated this issue also, but there was no evidence that the programme could in fact have been accelerated to any significant extent. Moreover, the Inquiry considers that the PFC was justified in continuing with its pasteurisation project into 1984: viral kill had been demonstrated to be higher than with dry heat treatment, and the ineffectiveness of the Hyland dry-heating process supported the choice of pasteurisation as the preferred technique.

The Inquiry also reviewed the position in relation to heat-treated commercial products, the first of which was the Hyland product referred to above. Further such products were licensed in the USA from February 1984, and used for specific 'named patients' in the UK after that date. Such products were not licensed in the UK until February 1985. The Inquiry concluded that there was no basis in the evidence for a finding that the UK licensing of commercial heat-treated product should have taken place before that date.

When the news came that HIV had entered the Scottish donor population, and that patients had acquired HIV from Scottish product, the PFC moved swiftly to introduce dry heat treatment and was able to provide the first comprehensive national supply of heat-treated Factor VIII in the world. The Inquiry has no criticism to make of those involved in viral inactivation in Scotland.

After 1984

It was to be more than two years before the PFC was able to begin issue of a Factor VIII product successfully heat-treated to inactivate NANB Hepatitis. The Inquiry investigated why this was so.

Developments elsewhere were examined to provide context. Commercial companies received licences in the USA from May 1986 for heat-treated products effective against NANB Hepatitis. As far as could be ascertained, the two products that were licensed in the USA before PFC's product, Z8, was issued in the spring of 1987 were not available in the UK. In England, the BPL was able to issue a Factor VIII product, 8Y, dry heated at 80°C for 72 hours, from September 1985. It was the first fractionator in the world to produce a dry heat-treated product which was NANB Hepatitis safe, although the quantities produced did not meet demand in England and Wales. At the time, it was not possible to demonstrate categorically that the product was hepatitis safe. Safety was only definitively demonstrated once the virus had been identified and tests for it developed, although empirical evidence to indicate such safety accumulated from 1985 onwards.

In 1985, scientists at the PFC were initially preoccupied with inactivation by heat treatment against HIV. Early in the year, they reverted to work on the pasteurisation project, although with awareness of progress elsewhere, especially in England. The PFC believed that the reason for the BPL's success in dry heating their product to a higher temperature related to its higher purity. Research at the PFC was itself concerned with producing a higher purity product, in order to facilitate pasteurisation. Adherence to pasteurisation was supported by rumours of HIV transmission by some commercial dry-heated product; in mid-1986, some commercial companies began to issue pasteurised product.

In the autumn of 1985, the PFC undertook some experimental work on dry heating Factor VIII at 80°C. It was discovered that the intermediate product could be heated to this temperature, but not the higher purity one. This result generated a realisation that the reason for successful high heating of the BPL product was the technique for freeze-drying, rather than the purity of the concentrate.

In December 1985, the PFC conducted a review of its viral inactivation work. It was decided to prioritise severe dry heating of the intermediate product, although there were still longer-term intentions in relation to pasteurisation. Further research work in relation to implementation of this decision took place in 1986. New equipment was needed for the freeze-drying element of the process. A pilot scale batch of Z8, the new severely-heated product, was ready in June 1986. It was envisaged that full-scale production could begin in September. But in August, a problem occurred with the freeze-drying, and it was not possible to adhere to the timetable. In October, product heated at 75° for 72 hours was produced; it was available for clinical trial in December.

At this point, a difficulty resurfaced regarding compensation for any harm suffered by patients trying the new product. The Haemophilia Director in Edinburgh had been concerned about this issue for some time, and now indicated that he did not feel able to try the product without the matter being resolved. The other Directors in Scotland agreed. The issue was a matter for the SHHD, in consultation with the Treasury. It took some months to resolve. The Inquiry considered that the time taken to resolve the matter was unsatisfactory, and that delay was caused to the clinical trials of Z8. In the result, however, there was no delay to the issue of Z8 to patients, since that did not commence until existing supplies of product were

exhausted. But there was delay in issuing the product for previously untreated patients, and adverse impact on specific individuals cannot be excluded.

In its review of this period, the Inquiry considered a number of points. The decision to adhere to the idea of pasteurisation remained justified; the goal of preparing a purer product was merited, and in the first half of 1985, appeared to be linked to the success achieved by the BPL in severely dry heating their Factor VIII product, 8Y. When the decision was taken at the end of 1985 to prioritise dry heat treatment, the period taken to achieve a product ready for clinical trial is not criticised. The possibility that the PFC could simply have copied the BPL process was explored, but it became clear that this would not have been a simple expedient: changes of process and equipment, involving considerable technical challenge, would have been involved.

Finally, the Inquiry considered whether the achievement of severely-heated Factor IX in 1985 implied that a Factor VIII product similarly heated could have been achieved at the same time. The differences between Factor VIII and Factor IX, however, giving rise to greater technical challenge in the treatment of the former, mean that this is not a valid comparison.

The Inquiry notes that the PFC's success in being able from 1987 onwards to provide all Haemophilia A patients with a product that did not transmit HCV was a considerable achievement.

Selection and screening of donors

The steps described above involved the treatment of blood products in order to kill any virus contained in them. It was not, and still is not, possible to treat whole blood or red cells to kill virus without destroying the therapeutic potential. The protection of patients receiving transfusions, therefore, depended on either preventing donors thought to be at higher risk of carrying infection from giving blood and, after each virus had been identified, testing donations to see if they were positive. Both in relation to selection of donors and screening of donations, the position differed for each virus. The Inquiry therefore investigated these aspects individually, in order to ascertain if steps which should have been taken were taken, and taken timeously.

Donor selection: hepatitis

The Inquiry investigated donor selection policies in the first part of the reference period, when the principal risk was the transmission of hepatitis. The main groups considered were intravenous drug users (IVDUs), prisoners and US military personnel stationed in Scotland.

In the 1970s, the prospects of identifying that an individual offering to donate blood was an intravenous drug user (IVDU) depended on general observation. If a donor had revealed a recent or current history of injecting drug use they would have been excluded. There was, however, relatively little face-to-face questioning of donors presenting at sessions.

In 1973, a World Health Organization (WHO) report intimated that Hepatitis B infection was associated with illicit drug use, especially amongst young men. In 1976, the International Society of Blood Transfusion (ISBT) issued guidance on groups of people who should not give donations, including suspected IVDUs. It was not universally followed. Guidance to staff in Edinburgh at that time was that a history of intravenous drug use required a temporary deferral of six months. According to some witnesses, questions about current

or past drug history became a feature of donor selection in the early 1980s, when there was a growing awareness of AIDS, although a leaflet in use in Glasgow in 1983 did not include any questions on the matter.

ISBT guidance from 1976 was that prison inmates should be excluded from being blood donors. In 1978, the WHO warned against certain groups donating blood, such as those known to have a higher than average prevalence of hepatitis. At this time in Scotland, as in other countries, it was known that there was a higher prevalence of Hepatitis B antigen in prisoners than in the general population. None of the Scottish or UK guidance documents on the selection of donors contained any reference to the collection of blood from prisons.

In the USA, opposition to collection of blood in prisons started early in the 1970s. But it was not until June 1995 that the Food and Drug Administration (FDA) issued a formal recommendation that current and recent prison inmates should be deferred from donation. In other countries, practice on prison blood donations varied.

The Inquiry gathered evidence regarding collection of blood in Scottish penal institutions; this is set out in the Report. Blood was collected from prisons in Scotland from at least 1957 up to the early part of the 1980s. Each region differed as to the date that collections ceased, with Glasgow being the last on 25 March 1984. The conduct of donor sessions in penal institutions was, as far as possible, identical to that of donor sessions elsewhere in the transfusion service. The Inquiry found no evidence that any additional steps were taken at prison donor sessions in Scotland to screen out higher risk donors, such as those who had ever injected drugs.

In May 1975, the Chief Medical Officer for England wrote to Regional Medical Officers in England, noting a relatively high risk of HBV being transmitted by the blood of prisoners. It was not necessary to discontinue the collection of blood in penal institutions, on condition that donations were subjected to one of the more sensitive tests available at the time. A copy of the letter was sent to the SHHD; the Deputy Chief Medical Officer (DCMO) intended only to discuss it with the National Medical Director of the SNBTS to establish practice in Scotland.

A workshop on hepatitis was held in Edinburgh in January 1981. A report stated that West of Scotland prison sessions had an increased incidence of HBV compared to the general donor population. The authors of the report added that the positive donors were not drug addicts, and the high incidence was probably related to 'social habits and hygiene'.

In June 1982, the Medicines Inspectorate questioned the collection of blood from prisons and detention centres in Scotland. The matter was discussed at an SNBTS Directors' meeting in March 1983, but it was not possible to agree a future policy. Individual Directors had the authority to run their region as they wished, and the National Medical Director had no power to enforce an overall agreement. Some Regional Directors, notably in the West of Scotland, relied on prison blood collections to remedy shortfalls in supply.

By May 1983, fears about potential AIDS infection in donated blood had become an issue. Use of donations from borstals and prisons was said to have ceased in England and Wales. Pressure to do the same began to mount in Scotland. By mid-August, collection had ceased in four of the five Scottish regions; the final prison session in the West of Scotland took place in March 1984.

The Inquiry examined what information was available at that time about the extent of risk in accepting donations from prisoners. In the 1970s and early 1980s, there was uncertainty about classifying prisoners as addicts, but there was clear evidence that some prisoners had been convicted of drugs offences and had admitted to having a drug habit. Annual reports were produced to Parliament on prisons and other penal institutes. These included data on the number of prisoners dependent on drugs at the time of admission. Evidence from the period showed a significant, and continuing, increase in drug dependency among prisoners, especially in 1983 and 1984. It was only from the 1981 report onwards that the authorities began to admit to an increasing number of prisoners with a history of drug abuse entering the system.

With regard to the blood supply, the percentage of total blood donations in Scotland collected from prisons fell from 2.38% in 1975 to 0.11% in 1984. It appeared to the Inquiry that ceasing to collect prison donations would not have caused an insurmountable problem with the blood supply.

The role of government in the policy of collection from penal institutions was also explored. Documents from the 1970s appeared to indicate that the Home Office favoured blood donation in prisons, as this allowed prisoners to make restitution to society. For Scotland, a former DCMO denied that the SHHD had considered the issue; decisions would have been left to the SNBTS Directors. Witnesses from the SNBTS agreed that donor selection policy was primarily for the SNBTS as transfusion experts.

On the question of whether collection from prisons should have stopped earlier, the evidence of SNBTS witnesses was explored, along with opinion from a leading transfusion expert from Finland, Professor Juhani Leikola. They were all of the view, with the benefit of hindsight, that blood collection from prisons was inadvisable and should have been stopped earlier.

In addition, the Inquiry addressed the possibility that the collection of blood from US military personnel in Scotland further increased the risk of infection. The donations collected from US military personnel between 1982 and 1990 represented, on average, 0.2% of the total number of donations collected annually in Scotland. The Inquiry is unaware of any evidence that the SNBTS knew, or ought to have known, that blood collected from US military personnel in Scotland carried a higher risk of transmission of hepatitis or HIV.

With regard to intravenous drug use, the Inquiry notes that even before the advent of AIDS in the early 1980s, it was recognised that evidence of current or past injecting habits was a reason for exclusion. The effectiveness of the system in Scotland for excluding such individuals from donation depended on the reliability and even honesty of the donor.

With regard to collection of blood from prisoners, it is apparent that practice across Europe differed. In Scotland, it is unfortunate that the SNBTS Directors did not consider whether it was appropriate to continue such collection until the matter was raised in 1982. It cannot be said, however, that if they had, they would have been likely to have stopped such collection, or that it was unreasonable to continue until the early 1980s, especially in view of the introduction of screening for HBV in the 1970s, the lack of information to suggest increased prevalence of NANB Hepatitis in prisoners and the perception that, in any event, the condition was mild.

In relation to the collection of blood from US military personnel, the amount of blood collected was very small, and there was no evidence that US service personnel presented a higher risk of transmitting HCV (or HIV) than the general Scottish or UK donor population.

Donor selection: AIDS

In Scotland, steps to discourage donors thought to be at higher risk of carrying the agent which caused AIDS were taken first in the Edinburgh and South East Scotland area. In March 1983, the Transfusion Director in Edinburgh read information about steps taken in the USA, and began work on a draft leaflet for donors. He drew on material from the USA and discussions with others locally, including a consultant in genitourinary medicine at the Royal Infirmary of Edinburgh. By the time of a meeting of SNBTS Directors on 24 May, he had a leaflet to circulate. It emerged that only very limited steps had been taken elsewhere in Scotland. As was subsequently appreciated, however, the problem of AIDS was greater in Edinburgh at that time than elsewhere in the country.

Over the next few weeks, the draft was revised. There had been some opposition to its terms. In carrying out revision, the aims were to avoid offence, to eliminate ambiguity and to reflect the most up-to-date information available. After meetings with interested groups and individuals, an agreed text was achieved. It asked individuals in any of the following groups not to give blood: men who had multiple partners of the same sex; intravenous drug abusers; Haitian immigrants to the USA; haemophiliacs; recipients of blood transfusion; and sexual contacts of people at risk. The net was cast widely because of the priority of preventing the transmission of AIDS.

The leaflet set out a list of people who could get AIDS. Included in the list were 'haemophiliacs' and 'recipients of blood transfusion'. The Inquiry noted a contrast between that statement, and the information being issued to people with haemophilia in May 1983.

In June, the SHHD became aware of the leaflet and planned to become more involved in the matter of composition and circulation. Before this, however, distribution of the leaflet commenced.

Meanwhile, a UK-wide leaflet was in preparation by the DHSS. It was released in Scotland, with an accompanying Press Release, on 1 September 1983. The Press Release included a line generally maintained by government at that time about there being 'no conclusive proof' that the disease was transmitted by blood or blood products. The leaflet itself, however, included the following question and answer:

Can AIDS be transmitted by transfusion of blood and blood products? Almost certainly yes.

Within the SNBTS, there were concerns among some about the effect of this publicity on donors. Across the UK, there was a lack of consensus about distribution of the material, in particular whether the leaflet should be sent to all donors. There appears also to have been fear that giving blood could cause a donor to acquire AIDS; one piece of material examined by the Inquiry was ambiguous in that regard.

By the end of 1983, the need for revision of leaflets was accepted. The Director of the transfusion service in Edinburgh began work to produce a revised version, which was available in January 1984. Throughout the year, the draft of a revised UK leaflet was circulated and discussed, with changes of text; a new version was finally issued in January 1985.

Other measures were taken in 1984; by June, there was a new SNBTS leaflet, which appears to have been issued in August 1984 and sent to donors in September. In November, the SNBTS started to require donors to sign a declaration that they had read the leaflet and

were not in any of the excluded categories. A leaflet issued by the Terrence Higgins Trust began distribution in December 1984. In that month, further revision of the SNBTS leaflet was also thought necessary. When screening of donated blood for HIV began in October 1985, a new leaflet was issued. Over all the revisions, the breadth of some of the excluded groups increased.

In retrospect, the single largest group to test positive for HIV in Scotland over the period 1984 to 1989 was intravenous drug users; 30% of the total in Glasgow and 53% in Edinburgh were IV drug users. It is not likely, however, that the people affected by the outbreak amongst drug users were also blood donors.

Review of these measures led the Inquiry to conclude that the steps taken in Edinburgh in 1983 were taken as soon as could have been expected, indeed those involved were prescient in identifying that action was needed. At times, areas of the rest of the country, particularly the West of Scotland, displayed a less constructive approach to these initiatives. The Inquiry observes that it is paradoxical that the Scots made faster progress with their leaflets because of the lack of government involvement; it appears that central government was hampered by the number of interests involved in the process.

In relation to the question of the prevention of donation by those who were at risk of transmitting the virus, the Inquiry did not identify other measures which should have been adopted but were not.

Introduction of screening for HIV

When the isolation of HIV (named HTLV-III) was announced in the USA in April 1984, it was stated by the US Secretary of State for Health that a test to screen the blood supply would become widely available within six months. Five US companies were provided with the method for mass-producing the virus in return for a royalty. But by the end of October 1984 no test to screen the blood supply was widely available, although field trials were ongoing.

Problems with false positive results from these tests were evident in the development phase, but US government agencies pressed on with attempts to introduce screening. The first test kits were licensed by the FDA in March 1985. Testing of blood donations was introduced in the USA in April. There appeared to be problems with the availability of kits. In the early phase of testing in the USA, significant problems of false positive results continued.

In mid-1984, the UK blood transfusion services were aware that testing of donated blood for AIDS would be introduced in the USA and there would be pressure in the UK to introduce screening. There was no licensing regime for kits in the UK. It was determined by the DHSS, however, that test kits should be evaluated before being recommended for use by transfusion services. This was partly influenced by the duty of care which the services were regarded as owing to their volunteer donors: false diagnosis of HIV-positive status would have adverse consequences for donors, and for the supply of blood.

During 1984, a UK HIV test was developed by leading virologists in London. It was used over the summer to ascertain prevalence of the virus in certain groups, including haemophilia patients. Government funding for the scale up of the test kit for industrial production was obtained in December 1984, and a contract for development was entered into with Wellcome Diagnostics. The tests in the UK and the US used different technology. The UK test did not suffer from the same problems as some of the first US tests.

Around the end of 1984 and start of 1985, attempts were made from within the transfusion service in Scotland to explore the possibility of developing tests locally, or becoming involved in evaluation of kits. No progress was made in relation to acquiring materials for development of tests. The SHHD was strongly opposed to the idea of the SNBTS doing its own evaluation of kits. It was content with the DHSS managed evaluation exercise.

The UK Expert Advisory Group on AIDS (EAGA) was set up in January 1985, and agreed that a screening test should be available in the UK as soon as possible. The SNBTS Directors agreed at their meeting in February that SNBTS proposals should not be pursued at this time. Arrangements for the UK evaluation were progressing by mid-February 1985. It was seen as important that testing began simultaneously throughout the UK.

Amongst haemophilia clinicians, there was anxiety at the delay in commencement of testing of blood donors. They thought an FDA approved test should be introduced immediately to test donations; a letter to this effect appeared in the *BMJ* in June 1985. There were divisions of opinion amongst interested groups, depending on their focus on donors or recipients of blood. In Scotland, Factor VIII was already heat-treated to inactivate HIV.

The evaluation process continued over the summer of 1985. There was concern that individuals might present as blood donors simply to have an HIV test once it was available. The solution adopted was to ensure that there were alternative sites where worried individuals could be tested rather than presenting as blood donors.

The first round of evaluation was complete by 30 July 1985. The Wellcome kit was one of three recommended for use in blood transfusion centres. There was some suggestion in the media that the evaluation process had been delayed to allow Wellcome to catch up with the US companies. Two test kits (Organon and Wellcome) were chosen for the second round of evaluation. These two became available in Scotland in July or August 1985 for assessment. The West of Scotland service performed a mini-evaluation and preferred the Wellcome kit, but the test kit for actual screening proved to be less sensitive than the development version used in the evaluation.

The intention was to commence screening of blood donations in mid-October and this date became fixed by September. Wellcome was able to provide kits for routine donor screening in mid-September. A press release on 1 October announced the screening of UK donations. Blood that tested positive was not to be used, and would be subject to a second test and a confirmatory test at a Reference Laboratory. On confirmation, the donor would be contacted and called in for discussion and counselling.

Screening was officially introduced on 14 October 1985, although the SNBTS was testing donations before that date so all blood stock would have been tested by the start date. In February 1986, it was noted that the incidence of infection was one in 46,000, which was low in international terms.

No Inquiry witness disputed the need for a thorough UK evaluation exercise. It would have been irresponsible to have introduced US-manufactured test kits in the UK without evaluation. Whether or not to introduce testing in Scotland was a Scottish matter. The SHHD elected to follow the lead of the DHSS in relation to kit evaluation. It was unfortunate that the West of Scotland service was not able to participate in the early field test of the kits proposed in June 1984.

From early 1985, EAGA was the most influential group in the field of HIV/AIDS advice. Two SNBTS Directors were members and therefore involved in UK decision-making. The proposal in early 1985 that Scotland proceed independently with evaluation would not in reality have been practicable, and independent screening in Scotland was not feasible. If routine screening had begun in the UK with the first US kits in the spring of 1985, there would have been problems with the assay quality, as occurred in the US.

The Inquiry concludes that there is no legitimate criticism of the processes employed for the introduction of HIV screening on the grounds of delay. Screening was introduced as soon as reasonably practicable.

Surrogate testing for non-A, non-B Hepatitis

Where there is no test for a particular virus, it may still be possible to test for abnormalities associated with infection with that virus. This is known as surrogate testing. After the existence of NANB Hepatitis was demonstrated in the second half of the 1970s, there was a debate in the USA about whether to test for it with surrogate markers. A programme of surrogate testing was eventually introduced in the USA, but most European countries, including the UK, did not introduce it. In the end, the issue of whether to introduce surrogate testing was overtaken by the discovery of HCV, the identification of it as the cause of most NANB Hepatitis and subsequent introduction of a specific test.

In 2001, it was decided in the High Court in England that surrogate testing should have been in place in the UK from March 1988, when EU rules on product liability came into force. The Inquiry examined the reasons why surrogate testing was never introduced in Scotland.

Research groups in the USA had reported a correlation between elevated levels of a liver enzyme, alanine aminotransferase (ALT) in donors, and risk of NANB Hepatitis in recipients of their blood. Later research demonstrated an association between the presence of an antibody to Hepatitis B (anti-HBc) in donated blood, and an increased risk of NANB Hepatitis in recipients. As a result it was suggested that elevated ALT and/or anti-HBc might be useful surrogate markers for NANB Hepatitis.

There were two problems with the use of such tests on donors. The tests were, by their nature, 'non-specific' and there would be many 'false positives' where the result for the marker would be positive, but NANB Hepatitis was not present. This could result in needless rejection of blood donations. Also the tests lacked sensitivity, and would give rise to false negatives – because they were indirect tests, NANB Hepatitis might be present without giving rise to abnormal levels of the marker.

On the other hand, there was increasing knowledge of the potential seriousness of NANB Hepatitis and the arguments for introducing surrogate screening of donors grew in the USA. In August 1986 the American Association of Blood Banks recommended that donor blood be tested for ALT and anti-HBc from November that year. Surrogate screening was introduced in some centres in 1986 and was in place widely across the USA by 1987.

In Europe, the US decision generated debate. There was more concern about the interests of donors. The incidence of NANB Hepatitis was considered to be lower generally than in the USA. There was uncertainty about the value and effectiveness of the surrogate tests.

The situation in Europe was set out in a document compiled on behalf of the Council of Europe in 1989. By that time, Chiron had isolated a part of the Hepatitis C virus and a screening test was being developed. Routine screening of donations for ALT was said

to have been conducted in West Germany, Italy, Luxembourg, France, Switzerland and Malta. Studies were being conducted in four other countries with low incidences of NANB Hepatitis, including the UK.

There were concerns about the relevance of the anti-HBc test. There was no logical basis for the link between antibodies to HBV and the presence of NANB Hepatitis. The most plausible theory was based on lifestyle factors, that someone exposed to one blood-borne disease may be more likely to transmit another. It remains unclear why there was such an association.

In the UK, an MRC study of post-transfusion hepatitis (PTH) was published in 1974. It was regarded for many years as proof that the incidence of post-transfusion NANB Hepatitis was not a significant problem in the UK; the Inquiry's view is that its limitations meant that it could not offer such reassurance. Proposals for a survey of PTH were made to MRC bodies in 1979 and 1981, largely on the initiative of the transfusion service in Edinburgh. These were ruled out. A Transfusion Services Working Party on Transfusion Associated Hepatitis set up in 1982 did not promote the idea of a study; it is possible that it was overshadowed by the emergence of HIV/AIDS.

In 1984, a study of NANB Hepatitis in the West of Scotland was carried out. It concluded that around 29–40% of PTH cases could be prevented by ALT testing and 3% of blood donations would be lost. The study was not detailed enough to form firm conclusions, as the recipients of the donations were not followed up. It was concluded on the basis of reported cases that PT NANB Hepatitis was not a major problem in the region. These conclusions were used for several years to support the view in Scotland that PTH was not a significant problem; the Inquiry considers this unfortunate.

In 1986, the Directors of the SNBTS put forward a funding request to the SHHD for a donation screening programme. The SHHD was influenced by a second report from the West of Scotland that claimed surrogate screening would have little impact on the already low levels of PT NANB Hepatitis. As a result of this report, ALT testing of Scottish donations was not recommended within the SHHD, to the disappointment of the SNBTS.

Over the ensuing years, the issue continued to be debated in the UK. In March 1987, SNBTS Directors recommended the introduction of surrogate testing. The SHHD was not in favour of the proposal; Transfusion Directors in England and Wales also felt that research should be conducted first. The recommendation that testing begin was not accepted.

Between September 1988 and April 1989 a three-centre study was carried out in the UK. The final report was produced in November 1989. It was difficult to conclude how many of the donors with raised ALT or who were HBc positive would have transmitted NANB Hepatitis. The ALT test was non-specific because of the correlation with alcohol consumption and obesity. In effect, the question of surrogate testing had been overtaken by the impending introduction of the anti-HCV test. The Advisory Committee on the Virological Safety of Blood agreed in November 1989 that there was no case for using surrogate tests for NANB Hepatitis, given the need to evaluate the HCV tests.

From May 1987, blood products used in Scotland were successfully treated against NANB Hepatitis. The population at risk after that date was therefore those undergoing blood transfusion. It is likely that ALT screening of donors would have reduced the transmission of HCV to some extent, but it is impossible to quantify that reduction with any degree of accuracy.

In the period 1987 to 1991, there was never enough concrete evidence to justify a recommendation to Ministers that surrogate testing should commence. There were conflicting expert opinions on prevalence, seriousness and possible causes of NANB Hepatitis. It was too late by 1987 to initiate a useful large-scale prospective study of prevalence. The predictive value of a raised ALT level was limited. The deficiencies in the surrogate tests would have given rise to difficulties in counselling donors and in maintaining the blood supply. The Inquiry does not attribute blame for the fact that surrogate testing was not introduced.

Introduction of screening for HCV

With the discovery of HCV came the opportunity to develop a test to screen for it. It was later to emerge, however, that the virus has a number of different genotypes; characterisation of these variants of HCV continues today. What was first discovered related only to a section of one genotype of the virus, with the consequence that initial tests did not detect all cases of HCV. The first generation tests were most reliable in detecting Genotype 1, the main genotype in the USA where the tests were developed, and tended not to detect Genotype 3.

The announcement in May 1988 that the Chiron Corporation had discovered proteins from what became known as HCV coincided with moves in the UK to establish a committee on viral transmission by blood. The Advisory Committee on the Virological Safety of Blood (ACVSB) was set up to advise the four health departments in the UK and had its first meeting on 4 April 1989. Expertise represented included virology, transfusion medicine, fractionation, infectious diseases, epidemiology, and haemophilia treatment. The Committee was chaired by the Deputy Chief Medical Officer for England. When it began its work, the policy intention was that screening should be introduced simultaneously throughout the UK.

Meanwhile, in December 1988, the transfusion services for England and Wales and Scotland had also resolved to establish a committee to address the risks of virus transmission. Their committee, the Advisory Committee on Transfusion Transmitted Diseases (ACTTD), held its first meeting on 24 February 1989.

Between the dates of these first meetings and the introduction in the UK of screening of donated blood for HCV in September 1991, both committees met and considered various issues, of principle and practice, around the introduction of screening. It was obvious to the Inquiry that the period of consideration was long. In addition, in 2001, in a case before the English High Court, it was decided that failure to introduce screening more quickly was a breach of product safety requirements, which apply across the legal systems of the UK. Among the 25 countries referred to in that case, being other countries in Europe plus the USA, Canada, Australia and Japan, the UK and Ireland were the last two to introduce screening for HCV in donated blood. The Inquiry therefore focused this aspect of its investigation on why it took so long to take this step in the UK. Assistance was again obtained from Professor Leikola from Finland; this also provided an opportunity for a comparison of events in Scotland and the UK with a small country elsewhere in Europe. All donations in Finland were screened for HCV, with first generation test kits, from 1 April 1990.

After the announcement by Chiron in 1988, the SNBTS was quick to take action to try to obtain test kits. The first ELISA test for HCV was not however released until November 1989.

At that point, both in Scotland and in England, studies of these kits were commenced. These exercises were necessary not only to understand the mechanics of the tests, but also to assess their sensitivity (how many false negative results were produced) and their specificity (how many false positives were produced) in the local population of the UK. Further such studies were conducted over the period 1989 to 1991; the carrying out of these was a contributory factor in the overall time taken and, in relation to the final study, of debatable necessity.

It was evident that the policy decision to introduce screening was not taken by government until after it had been recommended by the ACVSB on 21 November 1990. The Inquiry studied the minutes of all meetings of this committee between 1989 and 1991. At the beginning of its work, members were unsure that HCV was the cause of all cases of NANB Hepatitis; later discoveries were to confirm that this suspicion was not unwarranted in that there was considerable genetic variability in the virus. Other issues which occupied the committee were the reliability of the test kits, whether approval from the FDA had been granted for the kits and whether there was any confirmatory test available. A confirmatory test would reduce the risk of false diagnosis, with all the concomitant distress that might cause, and also prevent unnecessary reduction in donated blood available for use. A true confirmatory test would rely on a different reaction as evidence of the virus from the reaction which was the basis of the screening test; in the early stages after the Chiron discovery, production of such a confirmatory test was difficult owing to the limited characterisation of the virus.

The Inquiry also considered the role of the ACTTD. There was some overlap in membership between the two committees, and it appeared, particularly at the outset, that they were both addressing the same issues. Around a year later, in order to prevent confusion between the committees, the Chairman of the ACVSB stipulated that its role was to advise Ministers on the virological safety of blood, with the ACTTD considering the operational implications of policy. The Inquiry concludes that there was a risk of confusion between the two committees, and that, in retrospect, a better model would have seen implementation of policy in the hands of a sub-committee of the ACVSB, rather than a separate body. At times, the ACVSB became involved in issues which related to the practical implementation of policy, apparently contradicting its own delimitation of the roles of the two bodies.

In reviewing the time taken to reach a decision in principle that screening should be introduced in the UK, the Inquiry concludes that the setting up of an expert committee was a well founded decision: as at 1988, there was no standing body in the UK suited to advising the government on the risks presented to NHS patients by transmission of viruses in blood and blood products. But in its deliberations, the ACVSB missed two opportunities to recommend the introduction of screening at an earlier point; this conclusion is fortified by evidence that individual experts, both on the committee and elsewhere in the transfusion service, formed the view in the spring of 1990 that the time had come to recommend the commencement of screening. It is the view of the Inquiry that a decision to recommend the introduction of screening should have been taken by the middle of May 1990.

The Inquiry also examined the issue of why it took 10 months after the decision in principle had been taken for screening actually to start. Although preparations were in hand in the individual transfusion regions in Scotland from the end of November 1990, progress slowed in the first half of 1991. The Gulf War was an unexpected development, and accounted for some of the delay at this time. There were also unresolved issues in England

and Wales as to how screening was to be funded. Against this background, the policy of a uniform start date throughout the UK was not altered, despite some areas being ready to begin considerably earlier than others. The delays over the period March to September 1991 in Scotland were exclusively a result of adherence to this policy.

The Inquiry identifies four steps which could have been taken and which could have led to earlier introduction of screening in Scotland. For that to occur in fact, however, would have required the responsible Minister in Scotland to depart from the policy of a uniform start date across the UK. It is not certain that that would have happened, but the Secretary of State for Scotland and his Ministers should have been alerted to the situation in order that they could take a decision as to the most appropriate course of action.

In the event, screening across the whole UK did not begin until 1 September 1991 although, within Scotland, it commenced earlier in some regions, due to their involvement in testing of kits or to a desire to have all components tested and ready for 1 September. The kits used were second generation and, therefore, more reliable in detecting all genotypes of the virus.

Information to patients

The reference period for the Inquiry's investigation saw an increase in the understanding of the transmission of viral infection by blood and blood products, and an improvement in the ability to diagnose such infection. The extent to which information about these developments was shared by doctors with their patients was a matter within the Terms of Reference and an important aspect of the Inquiry's work. It also involved an exploration of the ethical standards which prevailed during the period, in order to ascertain what the extent of communication should have been. The reference period was long, and as might be expected, rules and practice evolved during that time.

It should be noted that the context for most of the Inquiry's investigation of questions of information and consent was therapy with blood products. Informed consent for blood transfusion does not appear to have been a major issue for clinicians in the 1970s, although there was increased awareness following the emergence of AIDS in the 1980s. Consent has not been formalised in the UK and, in a surgical setting, has been regarded as part of the normal process for obtaining consent for the overall procedure. There is more general agreement that patients should be provided with information about transfusion: its risks, benefits and alternatives. The potential for communication in relation to transfusion, however, may be much less if there is life-threatening illness or injury.

The Inquiry proceeded on the written and oral evidence of patients and their relatives, doctors, nurses, other professionals and officials. Expert evidence was taken from the Director of Professional Activities at the British Medical Association (BMA) and from the Chairman of the UKHCDO; publications from the General Medical Council (GMC) and the BMA during the reference period were also examined. In relation to publications, there may be a debate about whether they represent innovation in practice, or reflect what has been occurring in practice for some time already; this point arose from time to time when written guidance was examined.

Many patients felt they were given little or no information from their treating clinicians about the risks of infection from their treatment with blood or blood products. The circumstances in which blood products were required varied. Most witnesses who provided

statements told the Inquiry they were not warned of the risk of infection with HIV or NANB Hepatitis from the blood products they received. Some felt that because they were not warned of the risks of infection, they were denied the opportunity to make informed decisions about treatment. Many patients complained they were tested for HIV or HCV without their consent. Many were unhappy about the manner in which their diagnosis was conveyed.

The clinicians' general position was that, in personal contacts with patients, doctors made every effort to communicate effectively in unprecedented circumstances. They considered that testing of blood samples without express consent was commonplace, and acceptable by the standards of the mid-1980s. They believed that the evidence suggested patients were in reality told their diagnosis; patients in receipt of bad news often fail to absorb the information.

To attempt to resolve some of this conflict, the general background to medical ethics during the reference period was explored in detail.

In 1974, the BMA produced a 50-page booklet on ethics. It reflected a paternalistic attitude to patients, an attitude which appeared to have persisted into the 1980s. Doctors told patients what they thought patients ought to know, and what they were going to do as doctors to treat them. Many doctors did not tell patients the whole truth, especially in relation to incurable illness. They felt a duty to be reassuring rather than honest.

The first BMA handbook on medical ethics was published in 1980 and revised in 1981 and 1984. It gave guidance through a list of generally agreed precepts, a style abandoned in 1988. The GMC published advice to doctors in 1980 in the form of a list of what might constitute poor practice and lead to allegations of misconduct. Nowadays, the GMC produces detailed advice on what constitutes good practice, rather than bad, and has developed the concept of patient autonomy in the area of consent.

As at 1980, consent to treatment was assumed, rather than explicitly obtained. In October 1981, the World Medical Association adopted the Declaration of Lisbon. This confirmed that a mentally competent adult has the right to give, or withhold, consent to any diagnostic procedure and the right to receive the information necessary to make his or her decision. BMA publications do not appear to have reflected the need for explicit and informed consent until 1988. In the 1988 BMA ethics guide, it was stated that the basic principle was that a patient gives consent before any investigation and treatment proposed by the doctor. The BMA issued a further edition of its ethics guide in 1993. In that publication, it was stated that, as a prerequisite to choosing treatment, patients had the right to receive information from doctors and discuss the benefits and risks of treatment options. It referred to partnership between doctor and patient, and the ideal of decision-making through 'frank discussion'.

With specific regard to HIV, the issue of testing without consent was the subject of debate in both the BMA and GMC over the period 1986 to 1988. The BMA initially adopted a policy allowing testing without consent, but this was reversed at an annual meeting a year later. In 1988, the GMC published *HIV and AIDS: the ethical considerations* and stipulated the need for patient consent to procedures undertaken. Specific consent was required for HIV testing, because of the serious social and financial consequences which might ensue for an individual from merely having been tested.

The question of consent to testing for HIV first arose in practice from the second half of 1984, when research assays were used to investigate the prevalence of HIV in haemophilia patients. In the early days of testing, many doctors believed that HIV antibody tests could be carried out without consent. They considered that the fact that blood samples had been given earlier for other routine tests meant implied consent to any test had been given. Patients were aware they were routinely tested for a panel of infections such as blood-borne viruses. Many doctors would have considered HIV to be amongst that routine group, especially in the early days when so little was known about it.

In relation to hepatitis, the evidence before the Inquiry indicated that very little was said to patients about what was then termed NANB Hepatitis in the 1970s and early 1980s. In the mid-1980s, HIV dominated thinking, and hepatitis was overshadowed by discussions about AIDS. Throughout this period, patients who had persistently raised liver enzymes were probably told that they had NANB Hepatitis but that it was not a serious condition.

Neither the GMC nor the BMA has produced specific guidance or rules on information about or testing for HCV. Broadly, as knowledge increased, bleeding disorder patients should have been told about the risk of infection with NANB Hepatitis and the changing understanding of the severity of the disease. The evidence before the Inquiry indicated that, once a test for HCV was available, most doctors would not have tested patients without consent, although some might have done so on the basis that it was simply a further test of liver function, which patients were used to having tested. The nature of pre-test information and counselling required was not comparable to what was necessary before an HIV test.

Overall, it appears that there has been a move from the essentially paternalistic culture in medicine to a relationship where the patient is fully involved in decision-making. The experience of AIDS appears to have accelerated the move, and the Inquiry considers that the effect of AIDS and responses to it have had a more profound effect on doctor/patient relationships than any other single event.

Issues regarding HIV

Warning of risks

The Inquiry heard evidence concerning the approaches in haemophilia centres in Scotland to warning patients of the risk of HIV transmission. No single common approach could be discerned. In the period 1982–1984, uncertainty about the nature and cause of the new syndrome of AIDS was widespread. In Glasgow and Edinburgh, patients who asked about AIDS in relation to haemophilia therapy would have been given information by clinicians, insofar as the then current state of knowledge permitted. At Yorkhill, from 1983 when a new Director was appointed, discussions appear to have been more proactive.

As indicated above, however, there was at this time no published standard of conduct for doctors in relation to AIDS. Before the autumn of 1984, when both the agent of transmission and the prevalence of the virus in haemophilia patients in the UK had become known, there is no basis for criticism of individual clinicians in relation to the provision of information about risk.

Immunological studies

Routine blood tests of patients with bleeding disorders had been undertaken since the 1970s. In particular, liver function in patients receiving concentrates was regularly

monitored. This was a core part of patient care, and it was not necessary to discuss its inclusion with patients.

In 1983, both in Glasgow and Edinburgh, samples from bleeding disorder patients who had received treatment with concentrates were investigated to see if there were immune abnormalities similar to those reported in haemophilia patients in the USA. Particularly in Edinburgh where, in contrast to the position in Glasgow, no specific consent to these investigations was obtained from patients, the revelation of this work has caused disquiet among patients and their relatives. Its labelling as 'AIDS study' has increased concern. There have been suggestions that it involved experimentation on patients. During the hearings, it was acknowledged on behalf of the patients, relatives and the Haemophilia Society that there was no factual basis for this suspicion, and the Inquiry reached the view that any such suspicion was without foundation.

The Inquiry concludes that it was in the best interests of patients to conduct such studies of immune function. There was, however, no structured or systematic approach to providing relevant information to patients. The studies lay on the boundary between treatment and research. While aspects of the conceptualisation and implementation of the study could have been handled better, there was at that time no fixed rule which would have required consent from patients, and it is not therefore possible to say that breach of any ethical rule occurred. The same conclusion was reached in relation to the publication of the results of these studies in *The Lancet*; the data were fully anonymised and there was no likelihood of individuals being identified.

Testing of blood samples for HIV

The evidence indicated that, once tests became available, samples of stored blood from haemophilia patients at Glasgow Royal Infirmary were sent to Dr Gallo in the USA to be tested for HIV. Of the samples sent, 16% proved positive. It is likely that these results were available in August or September 1984. The Inquiry was not able to ascertain how testing of samples from Yorkhill was carried out, although it is evident from statements made at a joint meeting on 29 November 1984 that it had occurred.

Samples from patients in Edinburgh were sent to Professor Tedder in London and tested; again, some proved positive, with the results being available by the end of October 1984.

The patients to whom the positive results related were identifiable. The question therefore arises of whether it was ethically acceptable to conduct these tests without their consent. As previously noted, there was no explicit professional guidance on HIV testing at the time. It is therefore relevant to examine the position of the UKHCDO, the professional group. As at December 1984, the UKHCDO still regarded communication of a test result as discretionary; it therefore follows that they did not regard involvement of the patient in the decision to test as mandatory. It is clear that the testing of stored samples would not be acceptable today, and clear that standards were different in 1984, when much of the initial HIV testing of patients with haemophilia occurred without the knowledge of the patients concerned.

The Inquiry examined the case of a haemophilia patient in Glasgow who was tested for HIV in November 1985 without his knowledge. A sample of blood was taken at an outpatient appointment and submitted without the patient's consent. At the follow-up appointment, when the positive result was imparted, the patient was angry, which the Inquiry regards as entirely understandable. Although by that time, there was a policy

in place at the Glasgow Royal Infirmary for pre-test counselling and the obtaining of consent, this case demonstrates that it did not always operate.

Communication of results

The receipt of positive test results raised the issue of informing patients of their HIV-positive status. The GMC guidance of 1988 was that any doctor discovering a patient was HIV-positive had a duty to discuss these matters fully with the patient. The position before that was not explicitly set out in guidance.

In Edinburgh, no steps were taken to communicate test results to patients in the period immediately after discovery. Even by the meeting of Haemophilia Reference Centre Directors on 10 December 1984, nothing had been resolved. It was the view of that group that whether to impart a positive test result to a patient was a matter for the individual clinician to decide. The day after that meeting, the Edinburgh Haemophilia Director was contacted by a journalist wanting to report the story; evidence suggests that the news that patients in Edinburgh had been infected with HIV must have been leaked by someone to whom it had been imparted on a confidential basis.

The newspaper concerned agreed to defer publishing this information for one week. Immediately, a meeting was organised to take place at the Royal Infirmary of Edinburgh, in order to divulge to patients that positive test results had been obtained. It was not clear to the Inquiry whether patients from other haemophilia centres in Scotland attended this meeting; on balance, the conclusion reached is that Glasgow patients were not there.

Evidence of what occurred at the meeting was available from some who were there, but the most reliable material was from contemporaneous notes taken by the wife of a patient, who herself attended. It was communicated to those who were there that some haemophilia patients in the UK were positive for the antibody to HIV. Edinburgh patients were told that they could be informed if they had the antibody. More general information about the virus was communicated, the prospects for heat treatment of concentrates were referred to and precautions to prevent the virus being further transmitted were explained.

It was apparent to the Inquiry that, although some patients at the meeting understood that they, personally, might have the virus, others did not. There were reasons why this might be so: the Inquiry concludes that such a meeting was an inappropriate way of conveying such news and any advice consequent upon it, although media pressure at the time probably left little choice.

The follow-up to the meeting was that a letter was sent to haemophilia patients, inviting them to make an appointment to discuss their own position. It was clear that some patients did not discover that they were positive for the virus until some time later. The Inquiry examined the case of one patient who did not learn his result until January 1991 but, in the whole circumstances, including the contemporaneous medical records, is not critical of the physicians concerned.

In Glasgow, although the evidence was not clear, it appears most likely that in early 1985, HIV-positive status was not communicated to individual patients without that having been confirmed by a further test carried out. Patients were sent a letter dated 8 January 1985 on the topic of AIDS, with an appointment to attend the haemophilia centre; at such an appointment, the doctor would discuss the issue with the patient and, if the patient consented, take a fresh blood sample which would be tested for HIV.

The Inquiry considers that this process was preferable to what occurred in Edinburgh. An approach of offering information was reasonable, as a doctor could not force a patient to accept test results. But it was not made sufficiently clear to all Edinburgh patients that they had to ask if they wanted to know their own test result. Appointments could have been made for every patient. In the result, some patients did not learn their status until an extended period of time had passed. Some were angry; some were glad that they had not known. As time passed and questions of treatment became more relevant, greater proactivity in telling patients their results did develop.

More generally, the Inquiry notes that the news that their patients had been infected with HIV by treatment came after a period in which haemophilia clinicians had seen those patients' lives transformed by concentrates, and had rejoiced with them. In the early days of AIDS, doctors themselves were largely in the dark about the condition and could only pass on what little they knew. They had received no guidance or training for these unprecedented circumstances. Reassurance and comfort were offered, as was the prevailing ethic of the time, and were accepted by patients, who felt entitled to rely on what they were told. When such guidance proves wrong, it is inevitable that some patients would feel angry and betrayed.

Were a new disease like AIDS to emerge today, the patients would probably be made aware of the medical profession's ignorance of it, and share all the uncertainties and anxieties consequent on that. There would still be suffering, and probably anger against the disease, but the sense of betrayal would be absent.

Issues regarding HCV

The Inquiry examined practice in individual haemophilia centres and heard from clinicians and patients about the extent of communication regarding HCV. Much of the evidence from clinicians came in the form of general assertions as to what the position would have been. The recollections of patients that information was not given to them were sometimes contradicted by medical records. In both instances, establishing what conversations took place on specific occasions was almost impossible, given the passage of time and the imperfections of memory. That feature highlights the role that practice protocols can play, both in guiding professionals as to information which should be imparted and in generating a record that such discussion has taken place.

Warning of risks

The extent of the occurrence of NANB Hepatitis in patients treated with large-pool concentrates was not apparent until around 1978. By that time, monitoring of the liver function of patients at their outpatient appointments had become established. The material available to the Inquiry, including the *World in Action* documentaries in 1975, the circulars from the Haemophilia Society from 1978 and entries in individual patient records, revealed that there was a general awareness of the risk of hepatitis associated with concentrate therapy. It is less clear that patients understood the specific problem of NANB Hepatitis. At that time, however, and until the mid-1980s, the disease was not thought to be serious. Patients with elevated liver enzymes were likely to have been told that they had these results but that it was nothing to worry about. They may have been told that their condition was NANB Hepatitis, but the evidence before the Inquiry indicated that diagnosis of the condition was rare up to the late 1980s.

In any event, understanding before 1983 included the perception that UK concentrates were less likely to transmit hepatitis than commercial products from the USA. That perception changed with the publication of research indicating that the likelihood of contracting hepatitis from the first exposure to concentrates was close to 100%, whether the products were NHS or imported commercial ones. The risk was directly derived from the prevalence of HCV in the donor population; it is estimated that the prevalence in the general population of the UK over the period 1982 to 1984 was between 0.6% and 1%. Even then, however, the disease was not understood to be a serious clinical concern, and the risk/benefit analysis was still thought clearly to favour treatment of the bleeding disorder. In addition, during the mid-1980s, concerns about hepatitis were overshadowed by the issue of AIDS.

Insofar as individual centres were concerned, evidence indicated that at the Royal Infirmary of Edinburgh, patients who asked about hepatitis were given information about it, including by way of booklets. The policy of exclusive use of NHS concentrate was known by patients, as was its rationale, namely the affording of greater safety against blood-borne viruses. As knowledge of the potential seriousness of the illness increased, so too did the giving of information about it. A patient information sheet about Hepatitis C was issued in the early 1990s, after the virus had been discovered. At the Glasgow Royal Infirmary, according to clinicians, patients were routinely advised of the risk of infection by blood-borne viruses; in addition, the Inquiry was told that there were signs referring to hepatitis in the haemophilia centre as long ago as 1974. From 1985, when the risk of progression to serious liver disease was recognised, this was communicated to patients at reviews.

The position at Yorkhill up to 1982 appeared to have been that there was no specific discussion of hepatitis with parents. Quality of life for the boys was improved to an unrecognisable degree by concentrates and doctors did not realise that they were exposing them to serious viral diseases. The Inquiry was told that by the mid-1980s, however, parents were routinely informed of the risks of hepatitis.

Additional information about hepatitis was also contained in leaflets inserted into the packaging of Factor VIII and IX produced by the PFC from 1978, as well as on the vials of product. This information was primarily intended for clinicians, however, and did not obviate a need for them to tell patients about the risk of illness.

Factor concentrates produced by the PFC carried a risk of transmission of HCV until October 1985 (Factor IX) and April 1987 (Factor VIII). It was clear that practice varied in relation to warning patients of that risk, not only across Scotland but from patient to patient. In relation to assertions that patients were routinely advised of the risk, the Inquiry had evidence which tended to suggest that that was not universal in the centre concerned. It must be recognised, however, that for patients who were already established on treatment with concentrates, information about hepatitis was probably information about something which had already occurred. The crucial point for such information to have made a difference was before treatment with concentrates was given to a patient for the first time.

During the period concerned, information available about the risk was sparse and important details about the nature of NANB Hepatitis were not known. There was no published rule or guidance specific to the risk. In these circumstances, the Inquiry does not find any breach of ethical provisions in relation to warnings given or not given to patients.

Testing of samples; communication of results

The evidence before the Inquiry indicated that, once tests for the newly discovered virus were available in the early 1990s, haemophilia patients in Scotland were tested to ascertain if they had acquired it. In Glasgow, the HCV test was added to routine surveillance in late 1991. Patients were not tested without their knowledge and, if a positive result was obtained, that was imparted to the patient with such information as was available, and an assurance that their condition would be monitored. At Yorkhill the position was similar – patients were tested once tests were available, with verbal consent being given. If the result was positive, they were told on their next hospital visit and given leaflets from the British Liver Trust and the Haemophilia Society.

In Edinburgh, stored samples from patients were tested with the first generation HCV test, without the knowledge of patients. The testing was anonymous, however, and no criticism can be made of the process. Once the second generation kits were available, testing was repeated, this time on named samples. Patients were offered a further test, and the result of that was communicated to them. In some cases this may have led to unacceptable delay in imparting information to patients about their HCV-positive status.

In Dundee, a clinician new in post in 1992 discovered that stored samples from patients had been tested for HCV and the patients had not been told the results, despite there being a list of names of those who tested positive. It was not clear if their consent had been obtained for the testing. It was therefore necessary to explain this to patients; fresh samples were taken, testing was repeated and patients were told their results. Delay until 1992 in telling patients of their HCV-positive status after its discovery in 1989 was unacceptable.

Transfusion patients

The manner in which patients who acquired HCV through transfusion were told about it varied considerably. Many clinicians will have had little knowledge about the virus, and therefore diagnosis is likely to have been an anxious and distressing experience for patients. The Inquiry also heard from a witness who was diagnosed via the look-back exercise discussed below. Even then, and with the guidance issued by the SNBTS, little information was in fact given to this witness. It appears that there has not always been good communication or adequate information.

In relation to all the evidence about information concerning HCV, the Inquiry found the position to be similar to that which applied regarding HIV. There were complaints about information provided about the virus and about the manner in which diagnosis was communicated to individuals and complaints about testing without prior counselling and consent. Patients infected with viruses such as HIV and HCV required advice and information and should not have had to wait while the medical profession debated general ethical issues.

It was also apparent that, both in relation to HIV and HCV, anger and dismay had been caused to individuals by the discovery of infection and the realisation that clinicians had had information about their condition, or investigated it, without telling them. In the first half of the 1980s, people with bleeding disorders were confronted with the unprecedented circumstances of AIDS. In the second half of the decade, they were confronted with the reality that what had been presented as a treatment to extend life and improve its quality carried a risk of serious and potentially fatal disease. The resultant distress, anger and distrust were clearly demonstrated to the Inquiry.

Look-back

In the context of blood transfusion, the term 'look-back' refers to a process whereby, when viral infection is detected in an individual in circumstances which suggest others may also have been infected, attempts are made to trace those others. When the infection is identified in a blood donor on first testing, recipients of their previous donations are traced to ascertain if further infections have been caused. This is known as 'targeted look back'. When the infection is diagnosed in a patient and appears to have been acquired from blood transfusion, the donor is traced and, if possible, withdrawal of other components takes place. This is known as 'reverse look-back' and does not depend on there being a test for the virus.

There was early experience of look-back in the attempts made to ascertain how the patients in the Edinburgh Cohort had been infected with HIV. The 4000 donors whose plasma had been used to make the suspect batch of Factor VIII were identified. Owing to the fact that there were blood samples for only half of these individuals, however, and on expert virology advice, the exercise was not pursued. In late 1985 with the introduction of HIV donor screening, it was agreed that across the UK it would be accompanied by targeted look-back.

In 1990, a physician in the Edinburgh region of the SNBTS with previous experience of HIV look-back was asked to chair a working party to draft guidelines on counselling HCV-positive donors. He recommended that there should be targeted look-back in relation to donors found to be HCV-positive.

This recommendation was at odds with views which prevailed in the UK, including those held by senior figures in the transfusion services in Scotland and England. Opposition to look-back was influenced significantly by perceptions of the scale of the task. Both the ACVSB and the Medical and Scientific Committee (MSC) of the SNBTS decided against its introduction.

Despite this decision, the physician concerned proceeded with look-back in the Edinburgh area with effect from September 1991. It was suggested to him at the time that this work should be termed a 'pilot' or 'feasibility' study. In the early 1990s, there was debate about whether the availability of treatment created an imperative for look-back to be conducted.

Look-back was discussed at a further meeting of the SNBTS MSC in November 1993, but no policy decision was taken. On 18 May 1994, at an MSC meeting, a medical officer from the SHHD was present and reached the view, after hearing the discussion of look-back, that it was feasible, and that the fact that treatment was available for Hepatitis C might create an obligation to try to identify people who had been infected by transfusion. After that meeting, legal advice was sought by the SHHD; the advice indicated that it would be advisable to extend the policy across Scotland.

Over the next few months, the matter continued to be discussed by various bodies. The SHHD made it clear to the SNBTS that it could not go ahead until given the final instruction to do so, and indicated that it would be consulting with the Department of Health (DoH). Both the ACVSB and the ACTTD were also involved. The ACVSB met on 15 December 1994 and, after discussion including reference to potential legal liability in Scotland, recommended the imposition of look-back, giving no commencement date and stipulating that whatever 'is done should be done equally and uniformly throughout the UK'. On 22 December 1994, the Health Minister at the Scottish Office informed the DoH

that, in the light of medical and legal advice received, he had little choice but to carry forward look-back. In 1995, look-back commenced throughout the UK.

Research published in 2002 suggested that only a tiny minority of those exposed to HCV were identified by the look-back programme. For every patient identified and treated the benefit has, nonetheless, been considerable. Further, the National HCV Register has provided a uniquely valuable cohort which is starting to reveal long-term outcomes in very precise terms, and an ongoing study by the Health Protection Agency will show whether patients did benefit. The very act of undertaking look-back may also have improved the trust placed in the transfusion services by the public.

From a contemporary ethical perspective, the expert evidence available to the Inquiry indicated that the withholding of information from patients on the grounds of absence of treatment for a condition was not acceptable. The provision of a diagnosis could lead to life style changes, ensure new treatment could be given once it was available and prevent trust being lost.

The Inquiry answers in the negative the question of whether the rest of Scotland should have initiated look-back earlier than it did. In relation to the exercise required, the Edinburgh region had logistical advantages over the rest of Scotland. Further, although Interferon was thought to be a candidate for treatment from October 1993, there were doubts about its efficacy and it was not licensed for use until November 1994. It is not possible to conclude that an earlier decision on UK-wide or Scottish policy could have been reached.

The exercise across the UK was described to the Inquiry as one of the earliest comprehensive look-backs instituted in the world.

Final comments

The distribution of heat-treated Factor VIII concentrate from December 1984 and of heat-treated Factor IX from October 1985 ended the transmission of HIV by Scottish NHS blood products. Commercial products were also HIV-safe from around that time. Screening of donated blood for HIV all but ended the transmission of HIV by transfusion from 1985; there remained isolated cases of transmission by blood from donors who carried the virus but had not yet produced antibodies – the problem of donation in the so-called ‘window period’. Prevention of infection in the window period relies on donor selection criteria.

The heat treatment of NHS Factor IX introduced in Scotland in 1985 also rendered it safe against HCV. More severe heat treatment of Factor VIII introduced in 1987 inactivated HCV. The introduction of screening of donated blood for HCV in September 1991 all but ended the transmission of HCV by blood transfusion; as with HIV, there remains a small risk if donors who have been infected donate during the ‘window period’.

Blood transfusion continues today. The services publicise their donor selection criteria and are alert to new risks. The treatment of haemophilia is, however, different from that described in the Report; clotting factors are now artificially synthesised to produce drugs that do not carry a risk of viral transmission.

The legacy of the period when viral transmission via blood and blood products was occurring continues to be severe for many people, whether due to ill-health or loss of a loved one. There is one respect in which the Inquiry can recommend action to prevent

suffering from being greater than necessary – the detection of those whose transfusion-transmitted Hepatitis C infection is still undiagnosed. These will be people who received a transfusion of blood or blood components from a donor who was HCV-positive in the period before the introduction of screening for the virus and who acquired HCV but have not yet been diagnosed.

The Inquiry therefore recommends:

That the Scottish Government takes all reasonable steps to offer an HCV test to everyone in Scotland who had a blood transfusion before September 1991 and who has not been tested for HCV.

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