GRO-A

Tel: GRO-A

In Scotland haemophiliacs are calling for an inquiry into procedures which resulted in them becoming infected with AIDS/HIV and Hepatitis C. The Scottish Executive has always maintained that there was no negligence on the part of the Government, Scottish National Blood Transfusion Services (SNBTS) or Clinicians (Haemophilia Centre Directors); however, as there has never been an independent inquiry into the events of what happened I cannot see how this decision has been reached.

Although the Government, SNBTS and HCDs maintain that they always keep patients informed of any risks from the treatment of Factor concentrates as soon as they know, it seems that from the information obtained and from my own experience, speaking to other haemophiliacs and their families and from research documents this was not the case. Haemophiliacs **put their trust and lives in the care of the medical profession**, unfortunately for them, this was the wrong decision.

I have been told by the Scottish Executive that "... anything other than national policy was framed around a desire on the part of the clinicians to act in the best interest of patients – in the light of the knowledge available at the time." This has now been amended to "... The treatment given to haemophiliacs was provided in good faith ...", however the following states otherwise - That not just the clinicians but also the SNBTS and government could have and should have done more to protect the recipients of blood products (Factor VIII and IX).

NOT RELEVANT

The slowness in taking appropriate measures to prevent the contamination of the blood supply was in large measure the result of the rejection, or at least the non acceptance, of an important tenet in the philosophy of the public health: action to reduce risk should not await scientific certainty. When there was reasonable evidence that serious infectious diseases could be transmitted by blood, the principal actors in the blood supply system in Scotland refrained from taking essential preventative measures until causation had been proved with scientific certainty. **The result was a national public health disaster.**[2]

THE INFORMATION RELEASED DOES NOT ANSWER THE QUESTIONS
WHY

In **1982** when the Americans, Canadians, Dutch and other countries were alerting haemophilia patients to the risks of possible transmission of a **Fatal Immune Deficiency** from factor concentrates and recommendations were given about changes in the way haemophiliacs were to be treated. **Why** was nothing being done in Scotland to alert haemophiliacs?

Why were Haemophiliacs were never alerted to the potential **serious risks** which could be transmitted by blood products.

Why did the clinicians did not warn us about the **serious** and **fatal** risks of AIDS, when the risks became know by the beginning of 1983, and by this time haemophiliacs were being warned by the **possible transmission** of a **fatal immune deficiency** from Blood Products in other countries.

When in June 1983 the Council of Europe and World Health Organisation reflected the "**general awareness developed in the relevant and scientific and medical communities in both America and Europe of a significant and substantial risk that AIDS was caused by an infectious agent transmissible by blood and blood products**" and Recommendation R(83)8 was issued stating to ...

> **"...To inform attending physicians and selected recipients, such as haemophiliacs, of the potential health hazard of haemotherapy and the possibility of minimising those risks."**

Why was this recommendation never passed on to physicians and patients in Scotland, even after the UK DHSS passed the information on to Southern Ireland for them to act.

When donor exclusion warning were introduced in 1983 to notify blood donors of the risks of being able to spread AIDS, haemophiliacs and their partners were included in the group of 'high risk' donors. **Why,** by the time this action was taken, and haemophiliacs and partners were not allowed to donate blood, were haemophiliacs still not **informed** or **warned** of the risks.

In July 1983 AIDS had been found in spouses, (male and female, and siblings) of people with AIDS, it was well known by now that haemophiliacs contracted this disease as by now, there were haemophiliac deaths throughout the world, therefore, **why** did no-one inform us so that haemophiliacs could have taken steps to **protect themselves, their wives and their families.**

Why, by August 1983 when it was known world-wide about the threat of AIDS through blood products, did the HCDs decide it was better to '**allay fears'** (from my own experience that meant ignoring the question) rather than inform the patients, and again at a meeting at the end of 1983 when the question arose as to whether haemophiliacs should be warned about the potential dangers, HCDs and Management of SNBTS took the decision to risk not just the lives of haemophiliacs, but also the lives of our wives/partners, family and

friends, and **still took the decision not to inform us**, this decision was taken **after** haemophiliacs had by now become infected and died of AIDS in the UK, they still did not inform us of the known risks. Not to mention all the other meetings held in 1983 at which this subject was raised.

December 1983 "sufficient information was available to permit health authorities to make certain recommendations to inform ... **haemophiliacs**" this was correspondence from the Centre of Infectious Diseases to PFC. Was this information passed onto clinicians to inform their patients, (as it was the SNBTS/PFCs responsibility to inform clinicians of any dangers with their products), and **why** at this time was the decision to include the AIDS risk in package inserts not taken, by now package inserts on commercial products included the AIDS risk warning. **We are told that package inserts contain all adverse effects, including viruses, therefore why was the decision to exclude it from PFC products.**

Why when in **March 1983 an AIDS study was being carried out on haemophiliacs in Edinburgh** (and elsewhere in Scotland) were haemophiliacs never informed of the (by now known) seriousness of the risks of transmission from blood products, or indeed that an **AIDS study** was being carried out. The secrecy involved in conducting this AIDS study which was still being carried out in October 1984 when blood samples from haemophiliacs were tested for HTLV III (AIDS), patients were never notified that this test or any other test was being done for this purpose, and when the test came back positive, **why** at this time were we not informed. This was the time that it was recommended that patients who were HTLV III positive be **informed, reassured and counselled** to ensure that they understood what was being told to them, why this did not happen in Edinburgh

Correspondence from the Public Health Laboratory in October 1984 (copied to Dr Ludlum) asked "**Should the patient be told?**" ...Ideally I think he should ...This will be at the discretion of the local Haemophilia Centre Director." **Why** was the decision taken by Dr Ludlum **not to inform** individual patients of their HTLV III status.

By the beginning of 1985 patients throughout the world were beginning to be told of their HTLV III status, **personally and individually by their clinicians**, but the practice in Edinburgh was different, **why** were we not informed of our infection of HTLV III (AIDS) **until years later**.

Why were partners of haemophiliacs never offered a test as soon as it became available, or even when the haemophiliac was informed of his HTLV III status, again other countries were offering this test.

Whilst the government and SNBTS were issuing Donor warnings, offering counselling to donors before being HTLV III tested and then counselling donors with a positive test result, and offering their partners HTLV III tests and counselling, Edinburgh haemophilia Centre decided that their patients did not deserve the same treatment, therefore, **why** were donors given better consideration that the recipient of blood products in Scotland. Here in

Scotland, it seems we gave more thought into **not offending donors** than to informing Haemophiliacs of the known **fatal** consequences, why was this.

Counselling throughout England and Wales began in haemophilia centres in 1985, **why** did this not happen in Edinburgh.

From 1981 onwards it was well known in the medical and scientific community about the risk of AIDS from blood products, advice from many organisations stipulated that **haemophiliacs should be informed**, Government, PFC, SNBTS and clinicians all knew the risks of contracting AIDS from blood products, they all knew the **mortality rate was 100%,** and they all knew the routes of transmission, therefore **why** did no-one in Scotland take the time to inform and counsel patients of the serious risk and give them the **choice** of whether to use Factor VIII or not, before becoming infected, or indeed after. If information had been given, then this might have prevented at least **16 haemophiliacs in Edinburgh** from becoming infected**.**

HEPATITIS

We are told that no-one knew the seriousness of Hepatitis C (NANB), however documents released under the FOI state otherwise.

It was known in the 1970s that hepatitis could be and was transmitted by blood products, this disease was played down by clinicians, and patients were always led to believe this was a minor problem, however, **why** when in the **early 1980s** when it was stated in the medical and scientific literature that NANB could progress from **chronic persistent hepatitis** to **chronic active hepatitis** and **cirrhosis** within **6 years**, were haemophiliacs never informed.

Why were we never informed that NANB could be transmitted by sexual contact, this again put our **partners at risk**, according to certain documents, the seriousness of our partners contracting Hepatitis C in the **late stages of pregnancy** could be **fatal**.

In June 1985 it mentions that "few reports of death are attributable to liver disease ... **we predict that this will become more common**", therefore **why** were haemophiliacs not informed of this fact.

We are told that an AIDS fact sheet was circulated to patients; this fact sheet was not only informing haemophiliacs about AIDS and the precautions to take, but also about hepatitis, and the seriousness of it. Did clinicians check that all patients received a copy of this fact sheet, and was it explained that if you had not been informed that you had AIDS you still had to take the same precautions. Haemophiliacs were led to believe that if you were not told that you were HTLV III positive, then you were 'safe' to continue with your life as normal.

In 1986 when discussions about research into testing for NANB in Scotland it was decided to recommend research of "**no great significance or scientific**

interest because the prospect of research would serve to counter pressure from ... haemophiliacs and Haemophilia Centre Directors..." **why** was this decision taken.

Southern Ireland and other countries were by now being told that blood was being taken for a Hepatitis C test by July 1991. Again this was not the case for Scotland. **WHY**

By 1991 decisions were being carried out on how and what to tell donors, and it was decided "... What purpose is to be served by going back. Will it cause the recipient of the blood (**the 50% who are still alive after 2 years**) unnecessary stress ...could give **rise to litigation** ... **our Solicitors** ... guidance a little bit woolly respect of sexual intercourse ... Prof Tedder has published a paper stating that spread in this manner is a **definite possibility**". Haemophiliacs were never given the information that at least "50% of us would be dead within 2 years", or that "sexual intercourse ... spread in this manner...", **Why** were haemophiliacs not told that what was thought in 1991 was that "**50%" would be dead within 2 years**, could it be the fact that the clinicians, SNBTS, PFC and government were afraid it "**could give rise to litigation"** from haemophiliacs.

We have always been told that SNBTS and PFC products were the safest in the world, therefore, **why**, when their premises and practices were examined by the Medicines Inspectorate from 1981 to 1988 did they all **fail** the **minimum standards** for Manufacturing Licences and Product Licences - **why** were they allowed to continue production. – The Medicines Inspectorate Report states that "...**a licence would not be recommended for an industrial equivalent..."**

Documents released under the FOI state that "Only failure of the manufacturing process and QC could cause difficulty and cause damage to the patient. ... that risks have already been taken with patients lives. PFC has and is operating outwith the standards of the pharmaceutical industry ... PFC has manufactured product which has unequivocally endangered the lives of patients ... I have authorised the issue of products which failed to meet specifications ... clearly indicated that on the basis of breaches of GMP PFCs continued function rested on the provision of crown immunity."

When and **why** was **Crown Immunity imposed on the PFC in Scotland**? Was Crown Immunity imposed on PFC because they would not have received a Manufacturing Licence, and therefore a product licence, or was it to cover up practices which "**unequivocally endangered the lives of patients**."

The following are just a brief notes on "... knowledge available at the time." which were either found in documents released under the Freedom of Information (FOI), Lindsay Tribunal (Southern Ireland), Krever Report (Canada) or from papers which are in the public domain.

In **March 1984** a group of Haemophiliacs became infected with HIV/AIDS from a contaminated batch of Factor VIII manufactured by the **Protein Fractionation Centre (PFC)** in Scotland. This group of patients were always led to believe that "**it was just one of these things – that nothing was known about AIDS, and that nothing could have been done to prevent it**", however, for this group of haemophiliacs and the other **71 HIV positive** haemophiliacs (including children) in Scotland a great deal could have and should have been done to prevent their infection.

The following is just an example of what was known about AIDS and Hepatitis in the world and indeed in Scotland, the steps that **were** or **were** not taken to prevent transmission of infection, the donors, the facilities in which Factor VIII/IX were manufactured and the decisions taken at the time by clinicians, SNBTS and government which were contrary to **European Recommendations, e.g. Recommendation No R (83) 8** which the British Government passed on to **Southern Ireland**[1] to ensure that these patients were informed about the potential risk of AIDS, but it seems forgot to inform clinicians and patients in Scotland.

What was happening/being discussed throughout the world

AIDS

Concerns began to be raised by 1982 about the risk of transmission of AIDS through blood and blood products, it was stated by Prof Rozenbaum (at the trial of Dr Garretta [France]) that "it was clear in **mid-1982** that AIDS was of concern to haemophiliacs and patients receiving blood transfusions[2]". By July there were reports of cases of Pneumocystis carinii pneumonia (PCP) among patients with haemophilia A - Two had died; one remained critically ill - although the cause of the severe immune dysfunction is unknown, occurrence among the three haemophiliac cases suggests the possible transmission of an agent through **blood products**[3]. On 14 July the response to the NHF, (the US counterpart of the Haemophilia Society) and of the US public health authorities issued a "**patients alert**" which was printed in the bulletins of its local chapters and circulated to haemophiliacs, health professionals, and other interested parties[2], by August Dr Strawczynski, the chair of the Canadian Haemophilia Society's medical and scientific advisory committee sent a memorandum to All Directors of haemophilia Centres ... "Obviously" ... "we should avoid causing unnecessary anxiety ... **our patients should be informed and they must not feel that the information is being withheld from them**[2]". In November Dr L'age-Stehr (Germany) published a report about AIDS in the Federal Health Bulletin (Bundesgesundheitsblatt) entitled "**Unknown Pathogen the Cause of Fatal Immune Deficiencies?**" The authors documented the increasing number of AIDS cases observed by the

CDC since the middle of 1981, and stated that **recipients of Factor VIII concentrate were particularly affected**, and noted that AIDS appeared to be caused by an unknown infectious agent that was **transmitted through blood and blood products**[2]. This was again mentioned when in December "an infant is suspected to have contracted AIDS following **receipt of blood products** from a known AIDS case, adding support to the **infectious agent** hypothesis[1], at the same time treating physicians and the Dutch Association of Haemophilia Patients worked together to educate patients with Haemophilia about AIDS. Physicians at treatment centres recommended a number of changes in the treatment of haemophilia patients, organised meetings with their patients to discuss treatment options, and **discussed the risk of AIDS with the patients individually** ... Concern about the risk to haemophiliacs began in late **December 1982**[2].

In early **1983** doctors were well aware that the **virus giving rise to AIDS might be blood borne,** and the Irish Blood Transfusion Service Board (BTSB) shared in the general awareness, which developed in the first half of 1983 **of a significant and substantial risk that AIDS was caused by an infectious agent transmissible by blood and blood products,** and the Irish Haemophilia Society published a letter in their newsletter mentioning AIDS in haemophiliacs, while Southern Ireland **looked to The United Kingdom** Haemophilia Centre Directors **for guidance**[1].

In January 1983 Dr Cash (SNBTS) drew members attention to recent articles in the US, and also the Observer and The Lancet, about the problem of AIDS. A MMWR extract (CDC, Atlanta) had been circulated with this paper and Dr Ludlum informed members that in the UK a **questionnaire** had been sent out to haemophilia directors[4]. An article published in The Lancet on the 29th of this month stated "AIDS-like syndrome in two haemophiliacs in US ... this study suggests that **haemophiliacs may be at increased risk** of the acquired immunodeficiency syndrome and associated infectious or malignant complications. Careful observation of these and other haemophiliacs for appearances of symptoms will be necessary to further our understanding of this disorder[5]". The fact that there were few cases of AIDS in the Netherlands during the early 1980s did not deter public officials from recognising its potential impact. Beginning in 1983 the **Chief Public Health Officer** sent circulars to **physicians** about AIDS and helped finance efforts by the Dutch Association of Haemophilia Patients **to inform its members about the risk of transmission**. ... On the 27th February the Dutch Association of Haemophilia Patients wrote to its members to alert them to a possible connection between **factor concentrates and AIDS**[2], by March it was suggested that "**patients with haemophilia may be at increased risk of AIDS** ... Frequent blood-product use may increase the risk of AIDS[6].

In **March 1983 AIDS Studies began on haemophiliacs in Scotland**[7] (without their knowledge or consent).

In America this is the month that they issued a leaflet for blood donors entitled "**An important Message to all Blood Donors**", asking donors to refrain from donating blood if they were in any of the high risk groups – a list of groups

were set out and certain signs and symptoms of AIDS were given in the information leaflet[1], and this is also the time that Canada announced their voluntary self-exclusion for donors[2]. The first reported AIDS case in **Australia** was diagnosed in December 1982, but not confirmed until April 1983, and Dr Gordon Archer (Director) of New South Wales blood transfusion service issued a directive prohibiting homosexual men from donating blood as of 1 May because it was "**a virtual certainty that AIDS was already in the blood supply[2]. By** March 1983, **eleven** cases of clinical acquired immunodeficiency syndrome (**AIDS**) in **haemophiliacs** had been reported to CDC[8]**. ... Three** haemophilia patients in **Spain** were reported with AIDS[9].

Advice from the CDC ... steps should be taken to exclude **high-risk subjects from blood or plasmaphersis panels**. ... In the March issue of Annals of Internal Medicine three articles descried further cases of AIDS, and a fourth T-lymphocyte abnormalities, **in patients with haemophilia** ... **May be the submerged part of an iceberg** of which AIDS is the clinically obvious **"tip" ... the greater the exposure** to concentrates **the greater the risk** ... On the strength of 5 reported haemophiliac cases Deforges suggests that it is time to **consider giving up home therapy** programmes which are reliant on Factor VIII concentrates[10]. April is also the month that a repeat of the report of infant illness and AIDS to a wider medical and scientific audience, especially in Europe[1], and Dr Ll'age-Stehr described as "**alarming** the discovery of eight cases of AIDS in American haemophiliacs, and the results of three studies that had revealed a **significant decrease in the T-cells of haemophiliacs**[2].

Whilst information was being published in medical journals, and other countries were warning physicians and haemophiliacs of the "potential" risk of AIDS from factor concentrates, the United Kingdom Haemophilia Reference Centre Directors considered the situation in Britain regarding infection of Factor VIII - they discussed that there was **insufficient additional accommodation, equipment and staff** to change the production exercise in all regional transfusion centres[11]. – Therefore, they took **no action** at all. May is also the month that Dr Luc Montagnier and colleagues at the Pasteur Institute in Paris **isolate a new retrovirus**, lymphadenopathy-associated virus (LAV), believed to cause AIDS[2]., and the French published a circular about AIDS for distribution to blood donors, updating it in August to include haemophiliacs as a group at risk of contracting AIDS[2], and in Canada, the executive of the Ontario Chapter believed that many haemophiliacs were not receiving adequate treatment because **they were afraid of contracting AIDS**[2], and Heat-treated Factor VIII concentrate began in the United States[2].

Between **January** and **June 1983** the Committee of Ministers of the Council of Europe and the World Federation of Haemophilia meeting In Stockholm in June reflected the "**general awareness developed in the relevant scientific and medical communities in both America and Europe of a significant and substantial risk that AIDS was caused by an infectious agent transmissible by blood and blood products.** The recommendations adopted by the Committee of Ministers at the above meeting recommended to governments and member states: "**To inform attending physicians and selected recipients, such as haemophiliacs, of the potential health**

hazard of haemotherapy and the possibility of minimising those risks", and a recommendation was issued that blood donors be provided with information on AIDS so high risk groups could refrain from donating. Attached with the recommendation was a copy of the information leaflet which had been prepared by the American Red Cross[1], whilst the SNBTS discussed the attitude being taken by the American Red Cross and by the Council of Europe – Dr Cash (SNBTS) agreed to circulate copies of a Council of Europe paper on the subject of AIDS[12] while **Southern Ireland** furnished a **"Message to Donors"** to each potential donor and the Donor Registration form was amended to include a question "Have you read and understood the important Message to Donors?"[1] This is also the month when the first two **French** haemophiliacs were diagnosed with AIDS (LAV)[2], and at a meeting of the FVIII Safety Sub-committee on 15th June it was decided that "The putative 'AIDS' virus must be considered as a potential hazard in FVIII concentrates.[63]

In July there was documented link with blood transfusion and AIDS, whilst a memo from Dr Foster to Mr Watt (UK) mentioned ...This is consistent with the view that AIDS is a transmissible agent. ... Epidemiology strongly suggests a transmissible agent (i.e. **AIDS has been found in spouses, male and female, siblings, etc)** ... The AIDS victim is thought to be capable of transmitting the disease from **time 0** onwards ...Predicted mortality is **100% in 3-4 years** for those with **Kaposi's sarcoma** and **100% in 25 months** for those with **opportunistic infections** ... **Haemophiliacs are in the group which develops opportunistic infections** ... **Strong evidence for transmission by FVIII** ... For donor screening it was suggested that the presence of circulating immune complexes plus anti-HBc would identify **98.4%** of AIDS cases. Rejection on this basis would remove **10%** of all the plasma pool. ... still only seeing the **tip of the iceberg**[13].

By the Autumn a recent study had revealed that four out of every 1,000 Parisian donors were at risk for the disease; and that **the use of volunteer donors was no assurance of safety, given the large pool sizes**[2], and in the autumn of 1983 and early 1984 US fractionators **added warnings** about the risk of AIDS into the information in the product inserts[2], for haemophiliacs who were **still uninfected** in the autumn of 1983, the measures that **were and were not, taken were crucial**[2]. However, the policy of the Directors of the Regional Haemophilia Centres in the UK is to "**alley fears**"[1] – it seems that they just ignored the danger haemophiliacs were facing every time they injected themselves with Factor VIII/IX – this was at a time when SNBTS discussed first Haemophiliac death in the UK which was reported in the press,[14] and the information leaflet "AIDS and how it concerns blood donors" was published for distribution in Scotland by the SNBTS.[15]

A meeting of the UK HCDs took place on the 17th October and a reference to **two** cases of AIDS in persons with haemophilia in the UK ... at this meeting Dr Chisholm (Irish Consultant) raised the problem of patients refusing to take up commercial Factor VIII concentrate because of the **AIDS scare**[1] and in this month the NHF made available its revised recommendations on the prevention of AIDS in haemophilia patients.[16] By November dry heat-treated Factor VIII concentrate manufactured by Hyland is licensed in Canada,[2] and in

December of 1983 two cases of haemophilia and AIDS had been reported to the Communicable Disease Surveillance Centre at Colindale ... The authors suggest that the size of the pool of NHS concentrate has been increased to point where the benefit conferred by the use of volunteer donor plasma might have been lost. ... Heat treatment **may double** the cost of treatment to the British market ... **no evidence that any product, commercial or volunteer, is free from the risk of transmitting AIDS**.[17]

December 1983, "HIV first isolated,"[18] and this is the month that the UK finally discuss taking steps ... "Sufficient information is available now to permit health authorities to make **certain recommendations** that may decrease the incidence of AIDS among the groups that are at highest risk of acquiring the syndrome ... **Spouses** of AIDS patients have also been shown to be at an increased risk of acquiring the syndrome. ... **Informing persons with haemophilia and their physicians** of the potential health hazards of Factor VIII or IX products, **including the risks** related to AIDS.[19] SNBTS prepare batch of pasteurised Factor VIII for clinical evaluation. However, the first patient suffers adverse reaction and the clinical study is abandoned.[20] However, heat treated Factor VIII concentrates have been used by now without immunological complications being reported.[21]

By late 1983 and early 1984 discussions between haemophilia directors and senior managers of SNBTS in relation to the question of **whether haemophiliacs should be warned** about the **potential danger** of being exposed to HIV 1 infection from Factor VIII ... it was agreed it would **not be appropriate** because it would **cause unnecessary stress** to patients and result in **under treatment** of patients.[11]

By the time 1984 arrived, issues concerning haemophilia and the potential of sexual transmission of AIDS was discussed,[22] and the New England Journal of Medicine published a report of a study ... The investigators of the study concluded that blood components could transmit AIDS, that exposure to only one infected unit might result in transmission, and that donors who had developed no symptoms of AIDS could be infectious.[2]

In February 1984 Dr Ludlum said that in the treatment of children cryoprecipitate was preferred at present because of the **new danger of AIDS** ... Members discussed the reports from abroad which suggested that recipients of blood could also be at risk.[23] But unfortunately for a group of his patients who at this time were still HTLV III negative, Dr Ludlum did not inform them of the **new danger of AIDS.**

March 1984 is the time that HIV was **first cultured for research**[18] this is also the month that **16 haemophiliacs at Edinburgh Haemophilia Centre received an infected batch of Factor VIII.** The donor of this batch tested positive for vd.[24] – perhaps this donors sample was missed due to the "Antipathy towards the test by Centre Staff at Edinburgh and SE Transfusion Centre."[25] Samples from haemophiliacs at the Edinburgh Centre tested **positive for HTLV III** in October 1984.[18] Should the patient be told? Ideally I think he should, ... An alternative might be to inform the patient's spouse or

other close relative, ... This will be at the discretion of the local Haemophilia Centre Director.[26]

Haemophiliacs (including myself) were never informed that this or any other test for HTLV III was being carried out, nor were we at this time told of the results, (I personally was told of my results in **January 1987** the same time as my cousin, uncles and haemophiliac friends.)

Southern Ireland patients were contacted in November and asked to attend for the purpose of having a sample taken ... **particularly** patients with severe haemophilia ... These patients would have been **told** the sample was being taken for the purpose of a **HTLV III antibody test**.[1]

By December, "two notable recent episodes concerning UK concentrates ... HTLV III has been incorporated into at least one BPL and one **Scottish** batch of Factor VIII ... Recommended **patients be HTLV III Ab tested** ... Repeated if positive .. **Ab positive people should be informed, reassured and counselled** ... **Facilities only available for HTLV III Ab studies on contacts as part of organised projects.** Plastic aprons could be used for preparing and administering all treatments (including home treatment). Home treatment procedures should be reviewed.[27]

In 1985 Irish haemophiliacs were told of HTLV III results and HTLV III tests were offered to wives/partners,[1] unfortunately wives/partners in Edinburgh were never offered a test at this time, however, my wife did give a blood sample at the Haemophilia Centre under the guise of "**genetic research**", but I now think that this was an HTLV III test. **English patients** were also informed of HTLV III test results, counselling at haemophilia reference centres began.[28] - but not in Edinburgh. This is the year that "AIDS and the Blood – A Practical Guide by Dr Peter Jones was issued to Irish haemophilia patients.[1] This booklet was not issued to haemophilia patients in this country unless (perhaps) if you were a member of the Haemophilia Society, clinicians did not ensure that patients received a copy of this.

Donor testing began in June of 1985 – **Donors** were to be **notified** of being tested for HTLV III, **counselled** by BTS Staff if found to be positive. The BTS would take steps to trace recipients ... Inform the consultant responsible for care of the patient ... **All subsequent actions would be determined by the clinician**.[29] "It is essential that all individuals who are found to have positive antibody tests receive counselling in order that they may understand the meaning of the results and the other measures required to avoid transmitting the infections to others[30] ..." This was the information given out and implemented regarding donors, why was this not put forward regarding testing and informing haemophiliacs? And by November **contacts** of Canadian Haemophiliacs could be tested to determine whether they were infected with the disease.[2]

It was not until **January 1987** that patients at Edinburgh were informed that they were HIV+, and the manner in which they were told came no-where near the standard that was set for blood donors. I was given **No** counselling before

being informed of my HIV status and **No counselling** after, what I was told when I asked for the prognosis was according to Dr Ludlum that "he had more chance of dying of a heart attack, than I had of dying of AIDS." However, according to the Medical Research Council in October 1983 "**Hardly any patients lived for more than two years after diagnosis.**" It seems that as I was unknowingly tested in 1984, I was actually (according to MRC report) living on borrowed time. A test was **never** offered to my wife, and as I said no counselling before or after. But I was one of the "lucky" patients 'John' from BBC Scotland, Frontline Scotland Documentary "Blood and Tears" was not told for 6 years.

In September 1990, Mr Justice Badgery-Parker in the Supreme Court of New South Wales stated in the case against manufacturers and blood bank "It was well-recognised that blood products could transmit blood-borne viruses ... The risk in March 1982 could fairly be described as slight or remote though by no means far-fetched or fanciful. By **SEPTEMBER 1983**, the position had changed. There was a material risk of which the parents had not been previously warned. They **should have been** told about the AIDS risk but were not – and the absence of such a warning amounted to **NEGLIGENCE**"[30]

In October Lord Justice Bingham, (Appeal Court Judge) after ruling on whether haemophiliacs should gain access to documents held under Public Interest Immunity said "**grave errors of judgement were made**." ... "The tragedy was avoidable ... in the sense that, had different measures been taken in the 1970s and early 1980s, it could, at least in large measure, have been prevented."[31]

In the summing up of the Lindsay Tribunal it was said that "Doctors had an obligation to ensure that patients were told of their results **reasonably promptly** ... that those who have been tested and found to be HTLV III positive should be seen **as soon as possible** ... samples had been taken between November 1984 and March 1985 only started to be told the results in July 1985 ... **this was totally unacceptable**.

And in the summing up of the Krever Report it was said "the evidence of possible unacceptability of the blood does not have to be conclusive – the decision can be made on a basis of "**reasonable doubt**" as to its suitability. With reference to the AIDS problem in particular, the premise is not that the Canadian Red Cross has **to justify beyond any scientific doubt** that there is a link between the designated "high risk groups" and the **transmission via blood.** CRC has the **moral and legal obligation to protect the blood recipient above all.**

COMMERCIAL PRODUCTS

WHY when in 1978 the World Health Organisation and in 1983 the Committee of Ministers of the Council of Europe and the World Federation of Haemophilia **all** recommended that donor selection was of utmost importance, and all measure should be taken to prevent blood collections from risky

sources, and according to Dr P Foster in July 1983 ... "It was clear that many European participants were implying that **USA** products and/or plasma were **bad news**"[65] did Glasgow Western Infirmary/Royal Hospital for Sick children still purchase commercial Factor VIII up to and beyond December 1983? ..."During a full discussion, in which it was acknowledged that Glasgow Western Infirmary/Royal Hospital for Sick children appeared to be the last remaining hospital to use substantial quantities of commercial FVIII in the West of Scotland. ... Dr Mitchell should write to the consultants concerned why they needed commercial products. In addition Dr Cash would include the matter in a document which he was preparing concerning planning for self sufficiency in clinically safe product.

HEPATITIS

It seems that while haemophiliacs were finding out about the seriousness of AIDS, the clinicians forgot to inform us about another life threatening disease that we had already contracted from factor concentrates - **Hepatitis C** (non-A, non-B). We again, have been told that no-one knew the seriousness of this disease **before** the virus had been isolated, however, again the information we have obtained states different.

In 1974 "The existence of a **third** form of viral hepatitis, later referred to as **non-A, non-B** hepatitis, is postulated,[2] and from as early as 1978 there was a known risk attached to large pool (i.e. Factor VIII/IX) blood products – "Systematic screening of forty-severe haemophiliacs in Sheffield revealed **abnormal** liver function tests in thirty six **(77%)** ... A wide spectrum of chronic liver disease was demonstrated, including **chronic liver hepatitis and cirrhosis** ... The high incidence of chronic liver disease seems to be a recent development and **probably related to factor concentrate replacement therapy.**[32] Concerns were again being raised in 1982 regarding the risk of non-A, non-B - "Hepatitis is a complication of treatment remains a substantial difficulty ... The oncogenicity of the non-A, non-B group of viruses is unknown but the **possibility of risk cannot be ignored** ... Elimination of the risk of hepatitis in the treatment of haemophilia and related disease would represent a major step forward in the long-term management of these congenital bleeding disorders,[33] and the Haemophilia Directors considered a paper "Haemophilia Directors' Hepatitis C Working Party Report for Year **1980-81**" confirming that the "government were aware from as early as 1974 that the treatment with **blood clotting** factor concentrates carried a **risk of infection** with what we now know as Hepatitis C.[18]

Research was at this time being carried out on haemophiliacs **without their knowledge or consent** and in June 1983 discussions about research in the UK into non-A non-B hepatitis transmission in animal studies was put at risk because "we are likely to have a low priority for scarce animal resources and inevitably the work will be considerably delayed. ...On the credit side, it seems certain that commercial and/or government organisations in the US will already have planned similar experiments to those proposed by us (e.g. NANB or B viruses in FVIII concentrate and sucrose/glycine and

pasteurisation) and that the results of these are likely to be publicly available before we can make significant progress. **Whilst this is not a very satisfactory substitute** for testing sorbitol/glycine protection, **it could give us additional justification for proceeding directly to human subject testing**.[34] were the patients who took part in these studies informed that the UK had not tested on animals **before** they decided to proceed "**directly to human subjects**"? And by December 1983 it was noted that "The pattern of illness suggests that **more than one serotype** of non-A non-B hepatitis virus may be transmitted by Factor VIII concentrate prepared by the National Health Service.[35]

Between December 1982 and December 1983 a trial of haemophil T was carried out. This trial was to assess the attack rate of hepatitis and as a subsidiary to see if there was a reduction in severity, chronicity, type of hepatitis ... patients of any age were taken on for this study, the median age was 2, range 0.2 to 58; ... In summary, there was an attack rate of 70%.[36] As some of these patients were children, were their parents informed that their children were taking part in these trials, and was it explained to them about the risk of contracting non-A non-B hepatitis or indeed any hepatitis?

Hepatitis was discussed at meetings between SNBTS, and HCDs and at one meeting in February 1984 it was agreed that the reporting of incidence was good, in fact Dr Ludlum was collecting data on patients who **"go completely yellow."**[37] By December cryoprecipitate and DDAVP was recommended over the use of Factor VIII because of the risks – "In the UK unheated large-pool concentrates, even those prepared from voluntary donations have transmitted non-A, non-B hepatitis, and we learn that a first-generation dry heated concentrate has also transmitted the disease ... Cryoprecipitate (or fresh frozen plasma for haemophilia B) prepared from a small number of donors is recommended for the treatment of **children under 4 years of age and newly diagnosed patients** ... DDAVP is effective only in mildly affected patients with haemophilia A and von Willebrand's disease but is an **attractive option** in this group who are at high risk of infection from concentrates."[38]

In June 1985 an 8 year study of 79 unselected patients with haemophilia who had received clotting factor concentrates, there was evidence of **chronic progressive** liver disease in at least **17 (21%). 8** patients had **chronic active hepatitis** and **9 had cirrhosis** (**5** with oesophageal varices). ... Histological evidence suggested that non-A non-B hepatitis was mainly responsible ... Serial liver biopsies showed **progression from chronic persistent hepatitis** to **chronic active hepatitis** and **cirrhosis** within **6 years**, suggesting that chronic persistent hepatitis in haemophiliacs is **not as benign as hitherto supposed**. ... It is anticipated that liver disease in haemophiliacs will **become an increasing clinical problem in the future.**

Our observations show that **progressive liver disease is a potentially serious problem in haemophilia**. ... Serial liver biopsies showed progression of Chronic Persistent Hepatitis to Chronic Active Hepatitis and Cirrhosis within a period of **2-6 years**. ... We have probably **underestimated** the number of patients with **Chronic Active Hepatitis** and **Cirrhosis**. ... A

notable feature of our series is that 4 patients with Chronic Persistent Hepatitis have shown progression to Chronic Active Hepatitis and cirrhosis, this is at **variance** with the generally accepted view that **Chronic Persistent is benign and non-progressive** and leads us to speculate that repeated exposure to hepatitis viruses may modify the unusually benign course ... Although a **few reports of death** are attributable to liver disease in haemophilia have appeared, **we predict that this will become more common.** ... The introduction of virus-free or synthetic Factor VIII concentrates cannot be expected to make a significant impact for several years. ... **it is doubtful whether they will influence the progression of liver disease in those in who it is already established**.[37]

By July 1985 it was stated that "Clotting factor concentrates manufactured from thousands of units of pooled plasma are likely to transmit viral infections to haemophiliacs. The risk of post-transfusion hepatitis B is reduced but not abolished by screening donors for hepatitis B surface antigen (BSsAg), and HBV vaccination may reduce this risk even further. However non-A, non-B (NANB) hepatitis, with an attack rate close to 100% in haemophiliacs not previously exposed to blood or blood derivatives ... remains a formidable problem. ... 13 Haemophilia A patients who had not been treated previously with blood or blood products were given a dry-heated factor VIII concentrate ... Hepatitis developed in 11 patients (84%) and was invariable of type non-A, non-B."[38] and by the **mdi-1980s non-A, non-B hepatitis was known to cause serious disease, including cirrhosis and liver cancer** in a **significant proportion** of infected individuals. The **seriousness** of non-A, non-B hepatitis was one of the reasons that **surrogate testing** was implemented in the United States.[39] - By August it was stated that in the past ten years there has been increasing **recognition of** and **concern over**, the high incidence of abnormal liver function test results as well as markers for Hep B in haemophiliacs. ... Some recent evidence suggests **insidious progression on NANB hepatitis to Cirrhosis.**[40]

Certain clinicians and haematologists in this country had felt that the Transfusion Services had been slow to commence AIDS antibody testing and others had similar view in relation to NANB hepatitis surrogate tests. ... Hepatitis can be transmitted by blood and blood products, and is in Scotland an occasion but **serious consequence of blood transfusions**. ... Non-A, Non-B is not a specific disease but a heterogeneous collection of diseases. The hepatitis condition due to the Epstein-Barr virus and Cytomegalovirus are a substantial part of it. ... The case fatality rate is estimated in a textbook consulted by Dr Dan Reid at less than 0.1% **except in pregnant women, who are at much greater risk (10%) if they contract it during the last 3 months of pregnancy.**[41] This is one of the reasons WHY haemophiliacs **should have been informed** that they had non-A, non-B as there was a very great chance that they could have infected their wives/partners during pregnancy, which it seem could have had fatal consequences.

There was increasing evidence in the USA and several European countries were introducing Anti-HBc and/or ALT testing of blood donors in an effort to minimise the risk of NANB transmission through blood and blood products by

June 1986.[42] This was because of the growing concern that non-A, non-B hepatitis may represent a **more serious health hazard than previously thought**, and in September the American Association of Blood Banks announced that its members will begin screening all donated blood for evidence of non-A, non-B hepatitis.[43] However, in Scotland the position explicitly reached at the meeting in December is to ... recommended research **of no great significance or scientific interest** because the prospect of research would serve to **counter pressure from for example haemophiliacs and Haemophilia Centre Directors** to embark on an indirect and largely ineffective form of screening, which would also lose us a certain amount of perfectly harmless blood.[44]

By June 1989 the **emergence of significant morbidity and mortality in persons with haemophilia associated with long-term exposure to hepatitis viruses** in clotting factor concentrates has lost some impact owing to the emergence of AIDS in the haemophiliac population.[45]

Southern Ireland haemophiliacs began being told blood was being taken for Hepatitis C by July 1991.[1] This was not the case in Scotland, haemophiliacs were never informed that blood was being taken for non-A non-B hepatitis testing, just as they were never informed about blood being taken for Hepatitis C.

By the time **1991** arrived, discussions were being carried out on how and what to tell donors, unfortunately, for most recipients of factor concentrates in Scotland they had not been informed of Hepatitis C yet, nor had they been told that blood was being taken to test for it (although it was already known that they had non-A non-B hepatitis), but then again as the following states: **the 50% who are still alive after 2 years ...**", perhaps they thought that we would all be dead before having to inform us of the seriousness of having Hepatitis C, or perhaps they were afraid that **"it could give rise to litigation",** was it the decision of the "**Solicitors**" not to inform the recipients (i.e. haemophiliacs) making this a **legal** decision and not **medical**? "... In the present state of knowledge, donors who are only HCV seropositive donors without evidence of antigen may not be infectious. What purpose is to be served by going back. Will it cause the **recipient** of the blood (**the 50% who are still alive after 2 years)** unnecessary stress, worry and possibly distress. In certain circumstances **it could give rise to litigation** and it may be that you would wish to discuss this particular point with **our Solicitors** before this policy is put into effect. ... The guidance is a little bit woolly about the guidance to be given in respect of sexual intercourse and the possibility of infection being transmitted in this way. ... Professor Tedder has published a paper stating that **spread in this manner is a definite possibility.**[46]

In June 1997 when NBS asked hospitals to return the remainder of 2,222 blood products, one of which might contain a low level of hepatitis C virus the question "**How dangerous is HCV?** was asked. This is a question that haemophiliacs began asking when they were eventually informed that they were HCV+; however, very few (if any) received the answer: "... there is a realistic chance of the development of cirrhosis and/or cancer of the liver

which, without a transplant will probably prove fatal. The statement then goes on to ask the **Current position** only to be answered by "...Persistent HCV infection can cause chronic hepatitis which may progress, in some, to cirrhosis and liver failure or liver cancer, although frequently not until **20 years** or more after infection."[47] – But by now nearly all Scottish haemophiliacs have had Hepatitis C for 20 years or more, most cannot tolerate the treatment available which might clear the virus, therefore according to the above "a liver transplant" is the only option.

Testimony from a leading academic Eric Preston at the Lindsay Tribunal suggests it was known during the 1980's that NANB Hepatitis was a **serious virus**, and was transmitted by factor concentrates. In his testimony it says ... "Prof Preston reiterated his belief that in the late 1970s and early 1980s, it was known that NANB Hepatitis could progress. He accepted that there may have been two views, but it had always been his view that NANB **was progressive**. Prof Preston said that his views about the progressive nature of NANB Hepatitis would have been known to treaters of people with haemophilia and would have been discussed."

According to Raymond Bradley, one of the world's leading lawyers in this area, by the early 1980s it should have been appreciated that this viral condition had **serious medical consequences**.

INFORMING PATIENTS

In Scotland ways of informing patients of any risks to transfusions from blood products was great and varied, I personally can only speak of the procedure carried out in Edinburgh where I am a patient, and if this is an example of how patients were told throughout the country, then this alone **warrants a full public inquiry**, because it put wives/partners and family members lives at risk **– of this there can be no doubt**.

Clinicians in Scotland say that haemophiliacs knew of the risks from hepatitis, that hepatitis viruses were mentioned in the package inserts with the product, but haemophiliacs were always told that **hepatitis was not a serious disease**, they were **never** informed that it could be passed through sexual contact, and in this way put the lives of their wives/partners at risk, nor that it was progressive, and it **could be fatal**, it was always a disease that was played down. When non-A, non-B was beginning to be found to **cause chronic liver disease** and **cirrhosis** and ultimately **death**, clinicians should have began to warn patients of the severity.

Although patients **trusted** their clinician with informing them of any risks and clinicians say that patients knew of the risks of hepatitis due to the package inserts, the circumstances surrounding the informing of the risks of AIDS is a different matter.

Although from early 1983 it was well known in the medical and scientific community that AIDS was a risk to haemophiliacs, and these risks were

discussed at several meetings throughout 1983 and 1984 and in **June 1983** the Council of Europe issued Recommendation No R(83)8 and directed member states to inform haemophiliacs of the health hazards of haemotherapy – "**To take all necessary steps and measures with respect to Acquired Immune Deficiency Syndrome and in particular ... to inform attending physicians and selected recipients, such as haemophiliacs, of the potential health hazards of haemotheapy and the possibilities of minimising these risks.**"[53] Haemophiliacs in Edinburgh were **never informed** of AIDS or the risk it posed to them (and their families) through treatment.

In late 1983 and early 1984 SNBTS and HCDs discussed whether haemophiliacs should be warned about the **potential danger** of being exposed to HIV 1 infection from Factor VIII ... It was agreed it would **cause unnecessary stress**...[11] so they decided not to warn us, – This was after the Council of Europe Recommendation R(83)8, and at a time when US fractionators **added warnings** about the risk of AIDS into the information in the product inserts. By now, haemophiliacs **should have been warned**, this was the latest time that they should have deferred from informing patients, not only did they **know it could be fatal** for the haemophiliac, but also **fatal for close contacts**. Clinicians said that they did not know which patients were infected with AIDS by this time as there was no test for AIDS, but they should have warned patients of the risks so that they could take certain procedures and precautions to protect their families. The informing of patients of the risks would also have given the **16 haemophiliacs in Edinburgh infected from March 1984 the choice of whether they were prepared to take the risk of using blood products or not.**

A letter of which a copy was sent to Dr Ludlum in **October 1984** discusses the morals and ethics of whether to inform patients of the risks and goes on to ask "**Should the patient be told?** – Ideally I think he should, but this will depend on many factors, including the amount of anxiety concerning AIDS there is already present at the Centre, and the degree to which the patient is capable of understanding the situation,. An alternative might be to **inform the patient's spouse or other close relative**, as is done when patients develop malignant diseases. This will be at the discretion of the local Haemophilia Centre Director."[61] Dr Ludlum **never** discussed it with my wife, in fact when he did decide to inform me in 1987 he wanted my wife to **leave the room** before being prepared to discuss the topic of the meeting – fortunately for me she stayed. But it seems I was luckier than 'John' from 'Blood and Tears', he was **not informed of his HIV status until 1990**.

In December 1984 an article in The Lancet refers to counselling patients with HTLV III and highlights the importance of this as the virus may be transmissible to close contacts – "Ethical questions are raised by HTLV antibody testing of blood donors and haemophiliacs. An unenviable task will be the counselling of people with positive results – a task made all the more necessary by the **detection of virus in semen and saliva**..."[62]

In **December 1984** HCD Organisation AIDS Advisory document was sent to the head of all UK Haemophilia Centres telling them that the virus that would later be known as HIV had been incorporated into **one batch of Scottish**, and one batch of English Factor VIII. It advised doctors to **inform those found to be HTLV III positive, to reassure, counsel and advise them about transmission.** - The way that Dr Ludlum informed his patients that some had become HTLV III positive was at a general meeting in a lecture theatre, unfortunately it seems that he never got the message across correctly, because the patients and families attending the meeting thought that the patients who were positive had **already been informed personally and individually** by their clinician, and that we were just being told that there had been a risk, that the risk had passed as Factor VIII was now being heat-treated and this would kill the virus. Myself, along with my cousin, uncles and haemophiliac friends all thought that they had missed this terrible disease, and as clinicians were not prepared to discuss HTLV III at any routine clinics or when attending for treatment we (incorrectly) assumed that we were negative for this disease, unfortunately, for myself, my cousin and my two uncles in my family we were **all wrong**. It must be pointed out here that not all patients attending these meetings were HTLV III positive, and not all HTLV III positive patients were at the meeting.

Frontline Scotland were informed by Dr Ludlum that a fact sheet was sent out to all patients, did he ensure that **ALL** his patients received a copy of this, out of all my uncles, cousin, nephews, myself and other haemophiliacs I knew, no one received a copy of this fact sheet. According to Dr Ludlum at the Hepatitis C inquiry this fact sheet covered the risks of Hepatitis C, but as it was an AIDS fact sheet, if you were never told you had AIDS you did not think that the information concerned your way of life.

"It is essential that all individuals who are found to have positive antibody tests **receive counselling** in order that they may understand the meaning of the results and the other measures required to avoid transmitting the infections to others..." this was sent to Doctors from SHHD, therefore **WHY** were haemophiliacs in Edinburgh not informed.[64]

By 1987 it was well known that haemophiliacs were at serious risk from NANB Hepatitis, "**chronic active hepatitis and cirrhosis within 6 years ... become an increasing clinical problem**" therefore, **why** did Dr Ludlum not inform me (and others) of the serious risk of NANB hepatitis at the same time as AIDS, or was it just that he though that by the time information was released about NANB, **we would all be dead**.

We are told that as the package insert mentioned hepatitis, that was our being told of the risks and the seriousness of it, however, as not every patient was receiving home treatment, they would not have necessarily seen the package insert and package inserts did not contain any warnings of AIDS at any time before the end of 1984. How many people read the package inserts with any type of medication, haemophiliacs (just like the general public) **relied** on their clinicians to **inform them** of any side-effects or **health risks** related to taking any medicines. Was it not the **responsibility for the clinician** to ensure that

haemophiliacs **knew of the risks** from hepatitis and AIDS and inform them **individually and personally** – ensuring that they understood what was being said?

Donors began being warned about the risks of AIDS in September 1983 when an Information leaflet "AIDS and how it concerns blood donors" has been published for distribution in Scotland by the SNBTS. When testing for HTLV III began being carried out for blood donors, again they were informed about HTLV III, they received counselling **before** being tested, and then counselling **after** being tested, if they were found to be positive their **partners were offered a test**. Why was the situation different for haemophiliacs in Edinburgh, we were **never warned** in 1983, **never informed** in 1984/85/86, our partners were **never offered a test**, and **counselling was never offered until much later.** As for Hepatitis C, I was led to believe by a clinician at the Haemophilia Centre that the only way to tell if a patient had Hepatitis C was through a **Liver Biopsy**, and as I am a Severe Haemophiliac I did not take up the offer of this procedure (as previously mentioned, haemophiliacs died due to liver biopsies) The next time Hepatitis C was discussed with me was in 2000 when I started AIDS treatment. I have since found out that I tested positive for Hepatitis C in April 1992.

The Lindsay Tribunal states: ... "Doctors had an obligation to ensure that patients were told of their results **reasonably promptly** ... that those who have been tested and found to be HTLV III positive should be seen **as soon as possible** ... samples had been taken between November and March 1985 only started to be told the results in July 1985 ... **this was totally unacceptable.**

The Krever report states: ... "Notification was important for three reasons. First, persons who were infected and unaware of their infection could infect others. Second, it was important that those infected with HIV be made aware of their status so that they could take advantage of the treatments that became available and continued to become available. Third, persons who had been infected **had a right to know what had happened to them.**

TESTING FOR OTHER VIRUSES

Again, I say haemophiliacs have been told that they are always kept informed of any blood tests which are carried out on them, a letter from Prof Ian Franklin to Rt Hon Charles Kennedy mp gives a list of viruses that haemophiliacs have been tested for these are:

HIV
Hep A virus
Hep B virus
Hep C virus
Hepatitis delta (associated with hepatitis B)
Human parvovirus
GBV-C virus

TT virus

Most of the above viruses I have not yet been informed about, but according to my medical records there are other viruses which I have been tested for and never been informed about.

Epstein-Barr virus
Cytomegalovirus

SAFETY OF TREATMENT

Haemophiliacs put their **lives in the care of their clinicians**, they **trusted** them to inform them of how safe treatment was, whether it was before a patient took part in trials of a new or changed product or whether it was to be issued for routine clinical use, however it seems that even this was not to be taken for granted.

Heat treatment began in 1983, Scotland maintains that we were one of the first HIV safe self-sufficient countries for blood products, which is all very well, but what risks was taken with haemophiliacs lives, the following is a sample of what was carried out from March 1987 when PFC issued Z8 Heat-treated to 75°/80°C.

It was known by the end of 1985 that "...there were many concerns in the medical literature that heat treatment of Factor VIII **may cause adverse reactions** in patients, which, taken with our earlier experience of pasteurisation ... **freedom from adverse reactions could not be assumed.**"[54] However, when in 1978 when Z8 was being introduced to patients we were led to believe that it all went smoothly, however, that is not the case.

A letter written by Dr Ludlum (HCD) to Dr Boulton states ... "I am led to believe that the issue of Z8 to patients has begun. I was aware that the standard production **was** running short and that we had **agreed to discuss** the further **evaluation** of the new material ... **I do not recall that I agreed that patients should be treated with this material.** So far as I am aware it does **not have a Product Licence** from the CSM nor a **Clinical Trials Exemption Certificate**. I am unclear on what **legal basis** it is being issued and **who is responsible** for any adverse side effects. As you will be aware much greater responsibility in these circumstances lies with the clinician who uses the product. **Whilst it might be difficult, but not impossible, for a patient to prove negligence** ... As you know **one patient who received Z8 developed central chest tightness and I am naturally worried that this material has been issued without any agreed monitoring arrangements**. I am now faced with a **fait acomplis** over Z8. This has comprised my position and reduced the clinical options open to me; i.e. either to accept the situation **and hope for the best** or go over to the purchase of commercial factor VIII.[55] Dr Ludlum then issues his patients with a Trials agreement form to sign, the attached information sheet to this states ... "We still wish to evaluate the new

Factor VIII which is being issued on a trial basis and we hope you will agree to use it. ... I believe that this new Scottish Factor VIII **is as safe as any available in the world and I would encourage you to use it**.[56]

Correspondence from Prof Cash SNBTS states "...I was surprised to learn that you were not aware of the extreme shortage of the NY product by February – after having received my "**Russian Roulette**" letter in December. ... I am bound to express some **considerable concern** at the document you have prepared for your haemophilia patients. I cannot escape the conclusion that you are opening a Pandora's Box – giving the patient the option to decide which product he wishes to use. It is difficult for me not to conclude that the whole SHS plasma fractionation programme will become the **victim of the whims of a small group of patients. If this is the way we are going then I am bound to request access to your patients with a view to giving them some information about commercial products. Surely we don't want to go down this road?** ... We're taking every possible step to expidite the licensing of Z8.[57]

Correspondence from 'Duncan' to Mr Calder SHHD states "...Only failure of the **manufacturing process** and the **QC** could cause difficulty and cause damage to the patient...[58] However it seems ..."...In the clinical sense the only thing that **can go wrong** is the **manufacturing process** and since under our old procedure (still substantive for hospital pharmacies) the Medicines Inspectors do the same scrutiny as for a formal manufacturing licence... However I (and they) accept that presentational purposes over-rule the science. That being the case there can be no half measures. ... Factor VIII and all the other products which PFC make are not new medicines nor is their any new problems associated with their clinical efficiency or safety. **Only the failure of the manufacturing process and the QC could cause difficulty and cause damage to the patient.** Therefore if for these presentational purposes (and I concede that they are real and relevant) a formal product licence is required the MI are quite correct to insist that a formal manufacturers licence is also required. Otherwise we would stand logic on its head.[59] However, according to the following, it seems that risks have already been taken with patients lives. "... I believe that at the present time it is in the public interest that the senior management team stick closely together. ... Nonetheless, I am bound to put on record at the comments you have attributed to Duncan Macniven, for it is my professional view that **PFC has and is operating outwith the standards of the pharmaceutical industry.** The evidence for this can be summarised as follows:-

1. PFC has manufactured product which has **unequivocally endangered the lives of patients** ... breaches of GMP could not be ruled out.
2. There have been a **number** of occasions when **I have been called upon to authorise the issue of products which failed to meet specifications**. I have on many occasions since 1979, with Bob Perry's support, given authorisation, over the head of the QA Manager, **in order to keep supplies in place for the SHS.**
3. Unlike our sister commercial organisations we have received no instruction to clear all batches of PFC products ... **before we issue for clinical use.**

4. ... clearly indicated that on the basis of breaches of GMP PFC's continued function rested on the **provision of crown immunity.**
It is my earnest hope that in the months ahead our current collective public interest stance will be vindicated, ...[60]

The above is documents relating to Z8 were released under the Freedom of Information Act pertaining to Hepatitis C and NHS Treatment with Blood Products for the period 1970s to 1990s, this information was also submitted to the Hepatitis C inquiry, therefore I must come to the conclusion that HCDs, SNBTS, PFC and SHHD were playing **"Russian Roulette"** with haemophiliacs lives.

DONOR SELECTION, SCREENING AND MINIMISING THE RISKS

Before the advent of tests for HIV/AIDS and Hepatitis C, the main way for a blood transfusion service to protect its patients from infection was to choose blood donors carefully, unfortunately for recipients of blood products in Scotland the selection of blood donors was questionable.

As early as 1970 a well known scientist Richard Titmuss published a book called "The Gift Relationship" which **argued strongly** against the use of **prisoners as blood donors**, this book resulted in an international change of thinking about ethical blood policies

By **1971** because of the **high prevalence of hepatitis B in prisons**, the Canadian Red Cross Society **stopped** collecting donations from **prison inmates**[2] and in **1978** the WHO had advised that donor selection was of utmost importance, and all measure should have been taken to **prevent blood collection from risky sources** the report stated "...Countries with a low incidence of hepatitis should not use whole blood or blood products obtained from source material collected from an area in which there is a high incidence of hepatitis ... National health authorities shall develop policies designed to prevent the transmission of other infectious diseases based on the prevalence of these diseases in the donor population and the susceptibility of recipients to the same diseases."[49]

In America in **1982** ... Dr Dennis Donohue, the director of the Office of Biologics of the Food and Drug Administration, the federal agency regulating the blood system in the United States, met (informally) with representatives of the four US fractionators. He asked them not to use plasma collected by plasmapheresis in high-risk areas ... **not to use plasma collected from prisons** and not to use plasma recovered from blood donations collected in high-risk areas – All four fractionators complied with his request ... and by December Alpha wrote to haemophilia treatment centres stating that it did not use plasma collected from prison inmates because **prisoners were recognized as a high risk population**.[2]

In Scotland we were still taking blood from prisons in January 1984 and from borstals in March 1984, although the procedure was questioned by the

Medicines Inspectorate as early as **March 1982**, and discussed at meetings of SNBTS where "Dr Brookes **felt strongly** that donations **should not** be collected from prisons because of the **uncertainty about replies** to questions concerning health" by **September 1983** NBTS Directors were due to discuss the matter and the DHSS would wish to consult the **Home Office** who had been **anxious previously to encourage donation in prisons.** Directors felt that a blanket decision to cease visiting prisons would be a **mistake.**[50] The way in which prisoners and young offenders were checked was "to examine their arms for signs of injection."[51] This was at a time when AIDS and Hepatitis was a known risk by the medical and scientific communities throughout the world. However, here in Scotland the decision to continue taking blood from prisons and borstals for **2 years** after the Medicines Inspectorate alerted the SNBTS and PFC that it was not good practice

The decision to stop the practice of taking blood from prisons took **22 months**, and **24 months** for borstals, from when the Medicines Inspectorate advised against the practice. It is said that SNBTS followed UK guidelines for extracting blood, but this is a policy which should have ceased even before the threat of AIDS due to the risk of Hepatitis in prisons. The Scottish Executive has confirmed that there was no data confirming whether prisoners were, or were not, a high risk population during the 1980's, Whilst there was no test for Hepatitis C, internal documents released under FOI legislation prove that Hepatitis B was certainly more prevalent in prisoners. Research carried out from 1.9.80 to 31.8.83 states that "screening prison sessions resulted in detecting **10 times** more donations with **grossly elevated SGPT** levels compared to other sessions." ... "The vast majority of [drug] abusers with elevated ALT levels admitted being heroin addicts and a considerable proportion were prisoners."[52]

The following is an extract from "Hazards of Transfusion Therapy":
This is the appropriate time to consider certain controversial features of donor selection in respect of the transmission hepatitis by transfusion. It has been established that with any potential donor population, certain groups have a higher than average incidence of HBs antigenaemia. In particular, HBs antigenaemia is more prevalent in **male prisoners**, and in volunteers from tropical areas. Some transfusion services have declined to accept volunteers in prisons and among immigrant populations. This ultracautious approach may be doubly undesirable. Few transfusion services have so much donor blood available that offers of substantial help can be refused in blanket fashion. Indeed visits to prisons to collect blood can often be arranged when the general intake of blood is low because of the holiday season. The incidence of HBs antiganaemia among male prisoners in Scotland is less than 1 percent using the most sensitive techniques of testing thus generous offers of useable donations would be lost by placing a total embargo on prison donors. Furthermore, it is **socially and psychologically undesirable to exclude prisoners** and donors from tropical areas from the donor population. **Acceptance of prisoners as donors helps to rehabilitate, and some of these volunteers become regular donors after their release...**

Prisons are not the only place that SNBTS recruited high risk blood donors from. SNBTS collected blood from **American troops** and other personnel at the **US Naval base** at Holy Loch – AIDS was first discovered in Haitians and Americans. In 1984 there were **6000** Americans with AIDS, compared to 102 in the UK. It was one of the most highly infected populations in the world. Back in 1978 the World Health Organisation had warned blood services against taking blood from **high risk** populations.

The above practice of taking blood from prisons should have stopped by 1978 when WHO had advised that donors selection was of utmost importance, and all measure should have been taken to prevent blood collection from risky sources, or in June 1983 when the Council of Europe also advised about the importance of selecting donors from non-risk groups, but in Scotland we still collected from prisons until 1984 and US Bases – a high risk group – even after January 1984.

FACILITIES FOR COLLECTING AND MANUFACTURING BLOOD AND BLOOD PRODUCTS

The **World Health Organisation (WHO)** in **1978** highlighted the importance of proper facilities for blood processing – "**The premises shall be of suitable size, construction, and location to facilitate their proper operation, cleaning and maintenance in accordance with accepted rules of hygiene ... and in addition provide adequate space, lighting and ventilation for the following activities where applicable ... Processing and distribution of whole blood and blood components in a manner that prevents contamination, loss of potency, and errors.**"

Here in Scotland, haemophiliacs were being led to believe that the facilities in which blood was collected and the Protein Fractionation Centre were the best in the world, however, the Medicines Inspectorate Reports stated otherwise. The following is just a sample of the comments made in the reports.

Medicine Inspectorate report, following a visit to Aberdeen and North East Scotland Transfusion Service 24th March 1982 (Mr KJ Ayling, Mr D Haythornthwaite)

Contaminated blood transfused in error: "Storage Facilities ... This Centre suffers from a chronic shortage of storage space, hence one of the needs for a new facility. ... Access to this is via the Grouping Laboratory. It is hopelessly overcrowded. Erroneous issue from this store has resulted in **hepatitis positive blood** being transfused on one occasion, yet it is still not possible to physically segregate between **quarantined** and **cleared** stock and there is a danger of HBsAg positive blood being used."

Medicine Inspectorate report, following a visit to East of Scotland Blood Transfusion Centre, Dundee, 25th March 1982 (Mr KJ Ayling, Mr D Haythornthwaite)

Not licensed: Licenses held by the centre expired on 30 June 1981 and have not been renewed."

Blood from prisoners: "Brief discussions were also held on sources of donated blood. At the time of this visit the Inspectorate had not visited donor sessions with 'Mobile Teams'. However it would seem most unlikely that we could continue to endorse the continued collection of blood from such places as Prisons and Borstals."
This recommendation is based on the following:

(a) Prison Medical Officers are often not involved in assessing the suitability of donors.

(b) The increased risk of infection associated with prison populations and the increased risk of transmitting disease through such donations.

(c) The unreliable answers to the pre-donation questionnaire that can occur in such environments as well as the motive of some of the donors."

Dangerous storage: "Corridors were being used to store material as diverse as:
Product e.g. stable plasma protein solution.
Materials potentially contaminated with hepatitis.
Fresh frozen plasma on a temporary basis awaiting collection by the PFC van.

Medicines Inspectorate Report following a visit to Edinburgh and SE Scotland BTS, 10-11 March 1982 and 10-12 May 1982 (Mr DRS Warburton and Mr D Haythornthwaite)

A highly critical report:
"This proved to be a difficult Centre to inspect. This was caused partly by the Considerable changes in progress. There is no doubt that the **existing facilities for the processing and handling of blood are grossly deficient** and would have been **quite unacceptable**. It seems unreasonable to 'dwell' on facilities which will only be used for 3-4 months. ... A further inspection of Edinburgh will therefore be necessary within 6 months."
No licence: "The manufacturing licence for this Centre expired on 30 June 1981 and no application has been made for renewal."
Criticism of use of prisons and borstals: "The location of bleeding and type of donor. For example, whether **Prisons and Borstals were really** appropriate or necessary as a source material."
Other criticisms about manufacturing methods: "The surprising practice of retaining blood routinely at ambient temperature for up to 18 hours. Two new refrigerated vans have recently been purchased so presumably this practice can cease immediately. Certainly protocols should be established for this process. ... Edinburgh is a Centre which appears to do a number of activities '**differently**' from elsewhere. ...It is not suggested that a difference 'per se' is important but they might rank as '**query-able**'. ... Entry for staff and materials is via the back door where one is confronted with an **appalling mess** of rubbish which is totally inadequately controlled and removed. Whilst it may be very difficult to control the **cockroach** and **rodent infestation** in old buildings of this type, the **unacceptable health hazard** posed by the additional material in this area must be given continuing priority attention by the hospital authorities. ... **Hepatitis and Microbiology** ... the autoclaves located here

used for inactivating contaminated items still runs on a pressure guage (20 lbs for 45 minutes) and has not been checked or regularly maintained. ... Brief discussions were held over the matter of QC tests. Much reliance would seem to need to be placed of 'accrediting' the donor as per WHO guidelines." **"Existing facilities are quite inadequate and must rank amongst the worst seen anywhere."**

Medicines Inspectorate Report following a visit to PFC, Edinburgh 1st October 1981 (Mr KJ Ayling, Mr Haythornthwaite)

General Comments: Areas where progress towards acceptable levels of GMP are still not adequate are as follows: ...2) Unsatisfactory processing conditions. ...4) Unsatisfactory work flow patterns, which could lead to product mix-up. ...5) Unacceptable staff movements through production areas, which could lead to contamination of components and product. ... **The present buildings and facilities continue to fail to reach minimum standards of GMP, and a licence would not be recommended for an industrial equivalent** unless agreed upgradings were instituted as a matter of urgency. ...The use of a closed system for plasma stripping, pooling and crushing would substantially upgrade this part of the operation and lead to clearer starting material for extraction of coagulation factors and fractionation products.

Medicine Inspectorate Report following a visit to PFC, Edinburgh, after 6th April 1988 (Mr KJ Ayline, Mr ML Kavanagh)

Products unlicensed: "the site does not have a manufacturing licence. ... Factor VIII concentrate and Factor II, IX and X concentrate **were licensed** but their PLs have **expired**. Albumin solutions have never been licensed. It is planned to submit PL applications for the clotting factor concentrates and albumin products **within the next 12 months**. ... PFC has previously been formally inspected in 1979 and 1981 and a number of informal visits have been made by the Inspectorate, the most recent being a one-day visit by KJ Ayling and ML Kavanagh on 6 April 1988.

Matters of concern: Storage of albumin products following the 30°C incubation is in random areas which are **totally unacceptable** and not controllable. ... a crate of unidentified blood bags containing haemolysed cells was on the floor. ... Although a Wellgate hand-washing unit is provided, its use is optional, as is the wearing of gloves ... Masks and beard-covers are not worn in the Fractionation Area, even when working over open vessels or paste. ...ivlg was being over-sealed in a dirty, open area, not under LAF. Validation is not carried out against a planned, agreed programme. In some cases, proposed re-validation of autoclaves, pasteurisation and dry heat treatment of Factor VIII is **not performed to schedule**.

Post Inspection Summary: ...**The possibility of a future application for a Manufacturer's Licence was discussed and the inspectors indicated that such an application could not be supported on the basis of the present situation**.

The above is just some of the comments made by the Medicines Inspectorate regarding the facilities in which collection and processing of blood and blood products were carried out, it was quite noticeable that in **1981 the Protein**

Fractionation Centre failed to reach minimum standards of GMP, and a licence would not be recommended for an industrial equivalent and in 1988, The possibility of a future application for a Manufacturer's Licence was discussed and the inspectors indicated that such an application could not be supported on the basis of the present situation. It seems that even after **7 years** the PFC could not achieve the basic standards for manufacturing its products.

In Edinburgh SNBTS and PFC - A virologists nightmare and a viruses dream.

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