

SNBTS DOCUMENT REQUEST No:

**2010/00055**

**Witness Name : Dr Brian Charles Dow**

**Dated : 28 January 2011**

**THE PENROSE INQUIRY**

**Penrose Inquiry – Topic C1 – Hepatitis C – Unsuitable Donors**

**A16765 Issue in respect of which a statement is sought**

**Hepatitis C**

**The acceptance of blood from ‘higher risk’ donors, in particular:**

- a) prisoners; and**
- b) donors who had a history of jaundice, and who were negative for Hepatitis B when the existence of Non-A Non-B Hepatitis was known and its presence could not be excluded**

**Witness Statement of Brian Charles Dow (request of 20 December 2010)**

I, Brian Charles Dow (date of birth 24 July 1950) say as follows:-

The statement is segregated into sections on a personal background; then Prisoners; and lastly History of Jaundice.

Matters to be included in the statement

1. (1) is covered at paras 2-5, 9-18, 27-30; Conclusions are in (3);
1. (2) is covered at paras 15 and 18
1. (3) The report was submitted to SHERT in 1984 and findings updated in the completed PhD (sent to Penrose 26.08.10 2010-00018) –otherwise paras 3, 9 and 13 are relevant
2. is covered by para 4 – I was a co-author of the Barr et al paper (1981).

**Personal Background for the period 1974 - 1990:**

1. I obtained a BSc Honours degree in Bacteriology/Medical Microbiology at Edinburgh University in 1974. My honours thesis involved devising a radioimmunoassay (RIA) test to subtype HBsAg. This experience led to my employment in 1974 as a basic grade scientific officer with Scottish National Blood Transfusion Service (SNBTS), based at the Glasgow Centre located at Law Hospital.

On commencement, I was placed within the Hepatitis screening laboratory where I became involved with the routine screening for HBsAg and anti-HBs and also developed screening tests for tetanus and diphtheria antibodies. The main scientific aim was to produce an in-house RIA test for HBsAg. This involved purification of HBV from human plasma and using this material to obtain high titre antibodies for use in sandwich RIA assays. This process took several years with the resultant LawRIA HBsAg test only being used on ante-natal specimens (around 60,000 tests per year). Other tests were also devised to screen for high titre anti-HBs, low level tetanus antibodies and diphtheria antibodies and subtyping HBsAg and anti-HBs using mixtures of "in-House" and recycled reagents.

2. During 1979, Dr Mitchell, then director of the Glasgow centre, encouraged me to begin a PhD study on Non-A, non-B hepatitis in West Scotland with Dr Follett at the Hepatitis Reference Laboratory, Ruchill Hospital. On commencing this part-time PhD, it was obvious that some funding would be required to purchase the necessary tests and reagents. A grant application was made to the Scottish Hospitals Endowment Research Trust (SHERT) and this was successful. The SHERT monies lasted 3 years and the PhD was submitted in September 1985 when I was drafted back full time to run the HIV screening laboratory at the Glasgow Centre. By 1989, a research assistant, who was performing HIV confirmatory testing at the Hepatitis and HIV Reference Laboratory, developed leukaemia and I was asked to help out on a part-time basis. This period was around the time of the launch of the first generation Ortho HCV test and therefore I was involved with its evaluation having access to numerous patient groups as well as donor samples. This eventually led to the formation of an independent confirmatory laboratory (National Microbiology Reference Unit (NMRU)) for the entire SNBTS (and Northern Ireland BTS) based within the Regional Virus Laboratory at Ruchill Hospital under the direction of Dr Eddie Follett at the commencement of routine donor HCV testing in 1991.

3. The PhD which I performed utilised the "higher risk" groups such as prison and donors with a history of jaundice, together with surrogate tests such as serum glutamic pyruvate transaminase (SGPT) (equivalent to alanine aminotransferase (ALT)) or anti-HBc and investigated high risk patient groups including haemophiliacs, intravenous drug users, renal patients and other referrals to the Hepatitis Reference Laboratory. The aim of the PhD was to identify the agent(s) that caused the disease

and develop an assay that could specifically diagnose the disease. This aim was also being pursued by countless scientists throughout the developed world and all were doomed to failure until the Chiron Corporation developed their first assay. My PhD was to my surprise asked to be read by Dr Dan Reid (head of the Communicable Disease Scotland Unit, the forerunner of the Scottish Centre for Infection and Environmental Health, which latterly became Health Protection Scotland), Dr Forrester (SHHD) and Professor John Cash (SNBTS NMSD).

4. With regard to the acceptance of blood from various high risk groups, I had little influence other than using science to prove or disprove various assertions. Policy decisions were generally made by Directors at their confidential meetings or by Advisory Committees that influenced government.

5. SGPT (and ALT) biochemical tests rely on statistical distributions to indicate that 3% are always above the upper limit of normal (ULN). However the “gross” elevations of SGPT found in the low percentage of blood donors only indicated a mild hepatitis. These levels though were much lower than those found in either acute HAV or HBV infections (where levels in excess of 1,000 units were common). In the 1980s, the chronic nature of HCV had not been proven and therefore most considered non-A, non-B hepatitis to be relatively harmless. With regard to the use of prisoners and donors with a history of hepatitis, as we in Glasgow had used sensitive third generation HBsAg tests since 1975, it was felt that we had prevented the maximum number of post-transfusion hepatitis cases as borne out by the reduction in post-transfusion hepatitis cases reported to the centre.

6. With hindsight, HCV is a chronic disease, and the use of surrogate tests such as anti-HBc and SGPT (ALT) would have reduced the number of individuals infected with HCV through transfusion. The use of prisoners did help to maintain stocks of blood over holiday periods but again in hindsight these individuals were “high risk”. The use of history of jaundice donors has not really been established as a source of transfusion-transmitted HCV infection – this is partly as HCV is a mild disease (with regard to SGPT/ALT elevations) with relatively few infected patients actually becoming clinically jaundiced.

## **PRISONERS**

7. In 1974, on entering employment with the SNBTS, it was common practice, as in other UK blood services, to collect blood in prisons, especially around holiday times when donors seemed reluctant to volunteer. At that time blood was screened for the presence of syphilis antibodies (using a non-specific test – VDRL carbon antigen) and HBsAg and anti-HBs by counter immune electrophoresis (CIEP) or immune electro osmophoresis (IEOP) (Milne, Barr and Wallace 1971 Lancet 1, 77). It was already known (published in Wallace, Milne and Barr BMJ, 1972 1, 663-664) that the incidence of HBsAg from new donors who donated at prison sessions was higher than new male or female donors in the general donor population. Of 1835 institutionalised donors, 12 were positive (1:153) whereas other males was 1:803 and females 1:2019 – based on IEOP testing of 105,724 donations between October 1970 and October 1971.

8. When HBsAg RIA testing was introduced in 1975 at the Glasgow centre (then based at Law Hospital), the incidence of HBsAg remained high in prison sessions compared to the general population. In 1977/78, the West centre moved to reversed passive haemagglutination (RPHA) testing for HBsAg – a less sensitive and more subjective test. Use of a pooling system to pool screen RPHA-negative samples (in pools of no more than 10) was used on plasma destined for fractionation and around 4 extra HBsAg positive samples were found using RIA in a period of 1 year (reported in Barr, Dow and Macvarish 1979). This scientific report also highlighted that in the period when RIA was used as the main screening test, no confirmed HBsAg post-transfusion cases were reported. Therefore the use of sensitive HBsAg assays led us to believe that we detected all HBsAg positive donors (whether they were prison donors or otherwise).

9. I was not aware of the existence of non-A, non-B hepatitis in Scotland until 1979 when Dr Follett (Head of Hepatitis Reference Laboratory, Regional Virus Laboratory, Ruchill Hospital) had raised the issue with Dr Mitchell. During 1978, reliable RIA tests for hepatitis A virus had become available and this allowed the investigation of viral hepatitis to include screening for both hepatitis A and B – samples with negative results being potentially non-A, non-B hepatitis. Tests were performed on donors and hepatitis patients with histories of jaundice in an attempt to identify if non-A, non-B hepatitis was a problem in the west of Scotland. The subject was offered to myself to pursue with Drs Follett, Mitchell and Professor Norman Grist (Professor

Morag Timbury took over midway through the PhD following Prof Grist's retirement) as my supervisors for a part-time PhD at Glasgow University.

10. Papers by Aach (New Engl J Med 1981, 304; 989-994) and Alter (JAMA 1981; 246; 630-634) in the USA indicated that the use of ALT or SGPT (a liver enzyme indicating liver damage when found in the peripheral blood) and the hepatitis B antibody, anti-HBc (core antibody) tests could help identify potential donors that transmitted non-A, non-B hepatitis. A grant application was submitted by Dr Follett and myself to SHERT for monies to fund these tests as part of work for my PhD. The grant was awarded.

11. Also in 1980, Dr Bob Hopkins (a senior scientist in the Edinburgh BTS) was also researching non-A, non-B hepatitis together with a PhD student, Sonya Field. Dr Hopkins organised a Hepatitis Winter Workshop, held in Stirling University in early 1991, which was later published in a special copy of Medical Laboratory Sciences (the former journal of the Institute of Biomedical Sciences). My presentation at this workshop (Dow, Follett and Mitchell Medical Laboratory Sciences (1981) 38, 359-363) showed preliminary work undertaken as part of the PhD study. This included a small number of SGPT assays performed on prison and normal donor sessions.

Table 3 extracted from Med Lab Sci 1981; 38; 359-363

#### SGPT testing of blood donors

Category	Number tested	>35 SF U/ml (upper limit of normal (ULN))	>42 SF U/ml	>125 SF U/ml (3.5 times the ULN)
<b>Prison donors</b>	<b>352</b>	<b>8</b>	<b>6</b>	<b>1</b>
Other donors	164	1	1	0
Total	516	9	7(1.35%)	1(0.19%)

ULN= upper limit of normal

12. This showed that prison sessions had more donors with elevated levels of SGPT compared to normal sessions. At this workshop Stuart Houston (MLSO in Glasgow BTS) also presented data showing that the West of Scotland prison sessions had an increased incidence of both HBsAg and hepatitis B antibodies compared to the general donor population (Barr et al Med Lab Sciences 1981, 38, 405-407).

13. My director, Dr Ruthven Mitchell, was aware of the data collected through regular progress reports and scientific appraisals that were conducted on all scientific staff within the centre. Indeed Dr Mitchell used some of the SGPT data in providing a response to an International Forum in Vox Sanguinis (International Forum, Vox Sanguinis 44; 57-58). At that time 1402 donors had been tested with 48 (3.4%) having levels above 35 SF U/ml – only 4 (0.3%) of these donors had levels in excess of 125 SF U/ml and all 4 were found to be prisoners. Dr McLelland (the Edinburgh BTS director) also provided a response indicating that prospective studies into the use of ALT were necessary.

14. Prospective studies were considered within my PhD study. An attempt was made using heart by-pass surgery patients at Glasgow Royal Infirmary. From recollection, this study gave such a poor return with only 2 or 3 patients returning at or around 6 months post surgery. It was realised that a proper prospective study would have required active participation by all heart surgeons and their clinical staff, and using the 6 month timing would in retrospect, not have identified many people with non-A, non-B hepatitis.

15. Throughout the 1980-85 period, I performed SGPT testing on a sporadic basis. The use of prison sessions was intentional as they had already been shown to have a high incidence of HBV and as non-A, non-B hepatitis was also thought to be blood borne, prison sessions were an obvious target population as were haemophiliac, intra venous drug users and renal dialysis patients. By early 1984, media revelations regarding the number of intravenous drug users in Scottish prisons eventually led to no more blood being taken at prison sessions. This, however, did not prevent former prisoners, on release, coming along to donate at any of the blood sessions.

16. Working with both blood donor samples and patient samples, led to recognition of certain names within the PhD. A number (15) of prison donors with grossly elevated SGPT levels were also found in patient referral samples with a risk group of intravenous drug users (page 89 of thesis). These individuals were associated with anti-HBc positivity, indicating past HBV infection.

17. Table 4.3 extracted from thesis by Dow (already submitted to Penrose Inquiry Team August 2010)

## Range of SGPT results on different donor categories

Donor Category	Number tested	>35 SF U/ml	>92 SF U/ml	>125 SF U/ml
<b>Prison</b>	<b>5057</b>	<b>222 (4.3%)</b>	<b>49 (0.96%)</b>	<b>36 (0.7%)</b>
Others (normal)	4980	125 (2.5%)	4 (0.08%)	3 (0.06%)
Jaundice History	484	13 (2.6%)	1 (0.2%)	1 (0.2%)
Total	10521	360 (3.4%)	54 (0.51%)	40 (0.38%)

18. The prisons that were used for these studies included the following:

Prison	Comments
Lowmoss	Bishopriggs, Glasgow, Low category male
Glenochil	Tullibody, Stirlingshire, Male prisoners transferred from Barlinnie and Saughton. Young Offenders Institute (YOI)
Shotts	North Lanarkshire, Max security, male
Barlinnie	Riddrie, Glasgow, <4yr sentence, male
Dungavel	Ayrshire, male. Now closed
Longriggend	North Lanarkshire, male. Now closed
Maxwelton	YOI, near Dumfries. Now closed
Polmont	YOI, Falkirk

Within the PhD study, most of the donations that exhibited grossly elevated SGPT levels (>92 SF U/ml) were physically removed from the blood bank and the plasma separated and stored frozen for research purposes (most of these units are still frozen and stored in the NMRU freezer at BTS Gartnavel). By around 1993 (after HCV donor testing had commenced), samples from 32 of these units were tested in second and third generation HCV assays and also tested for the presence of HCV RNA by polymerase chain reaction (PCR). The results of this exercise were published in *Vox Sanguinis* (Dow et al *Vox Sanguinis* 1994; 67, 236-237). 26 of the 32 donations were confirmed HCV antibody positive and a further 2 were shown to be only HCV PCR positive (early HCV infection), with only 4 (12.5%) negative for HCV. In hindsight, therefore, SGPT testing of prison sessions using an elevated cut-off would have removed some potentially HCV positive donations.

19. A further study conducted by SNBTS on the first 100 donors found HCV positive after commencing routine donor HCV testing in 1991, showed that 51/90 (56%) had abnormal ALT levels (mildly elevated) (McOmish et al *Transfusion*, 33,7-13 1993). In

other words, 39/90 (44%) had normal ALT values and would not have been detected if ALT screening had been in place.

## **HISTORY OF JAUNDICE**

20. There are numerous causes of jaundice including hepatotoxic drugs, anaesthetics, alcohol as well as infectious agents. Wallace reported in 1973 (Wallace, BMJ 1973 2, 347) that a series of 5640 volunteers with a history of either jaundice or of contact in the past 6 months with a case of jaundice had been tested for HBsAg and anti-HBs. Four were HBsAg positive and three anti-HBs positive, giving respective incidences of 1 in 1410 for HBsAg and 1 in 1880 for anti-HBs. Using the same IEOP technique to test for the first time 123,102 acceptable donors, 145 (1 in 849) were HBsAg positive and 121 (1 in 1017) were anti-HBs positive. This showed that volunteers with a history of jaundice or recent contact with a case of jaundice did not have a higher incidence of positivity for HBsAg and anti-HBs, compared to donors lacking this history.

21. On entering employment at the Glasgow centre in 1974, the routine HBsAg and anti-HBs testing system was in place following the first Maycock report's recommendations. The second Maycock report was issued in 1975 and this allowed the abandonment of the need to screen donors for anti-HBs (unless looking for high titre donors for plasmapheresis) and the relaxation of deferring donors with a history of jaundice, so long as they were screened for HBsAg using a third generation HBsAg test (i.e. RPHA or RIA) and so long as 12 months had elapsed from recovery from the jaundice episode. As this was a Department of Health recommendation, I presume it was followed by all the UK blood services.

22. I was aware that the donor forms (termed "K form") which were completed at the session had a reference to jaundice history. In the circumstance where a donor admitted a prior history of jaundice then the year of that jaundice episode was written on the card. The hepatitis screening laboratory staff routinely performed totals of new and previous and male/female donors on all these cards. The jaundice history was examined on occasions when studies were performed.

23. Examination of all the HBsAg positive donors in the west of Scotland did not reveal a higher incidence of prior jaundice history. Wallace (having retired) wrote to

the Lancet in 1978 (Wallace Lancet 1978, 2, 1004) quoting the data from his earlier report but pointing out that “the absence of a history of jaundice may be inaccurate. It was not uncommon for an accepted volunteer who had denied having had hepatitis to telephone subsequently, in great agitation, the information that he had jaundice. Similarly closer questioning of a minority of donors found to be HBsAg positive may reveal a history of hepatitis, although this was denied at the time of donation.”

24. Crawford et al (Lancet 1979 2, 155) “447 HBsAg positive donors have been found in the West of Scotland since testing was introduced in 1970. 13 (2.9%) of these donors admitted to a history of jaundice. This proportion is very similar to the proportion (2.8%) of those with a history of jaundice among 228,631 donors in the active donor panel and to the proportion (2.6%) found in a sample of 7460 new donors who first gave blood in 1978-79.” Since January 1975, 193 (0.087%) HBsAg positives were detected in 222,249 donors who had no jaundice history, whilst 9 (0.14%) HBsAg positives were detected amongst 6382 donors with a history of jaundice.

25. When sensitive tests for hepatitis B (as well as HAV) antibodies became available in around 1978-79, then more detailed studies were conducted on the donor population to determine whether jaundice history was related to HBV, HAV or non-A, non-B hepatitis.

26. The first study was by Dr Follett (Follett, Barr, Crawford and Mitchell Lancet, 1980 1, 246-248) who tested various populations and came to the conclusion that “screening patients and donors with a history of jaundice for HBsAg in a low prevalence country such as Great Britain where hepatitis A is also circulating is unrewarding on two counts. Firstly the jaundice is much more likely to be due to previous hepatitis A infection than to hepatitis B infection. Secondly, the evidence indicates that HBsAg carriage is normally a result of a subclinical anicteric infection.”

27. The second study (Barr et al BMJ 1982, 285, 1201) examined a total of 173 donors with a history of jaundice and testing them for anti-HAV, anti-HBs and anti-HBc. 17 (9.8%) gave negative results with all three antibodies indicating that their jaundice may have been caused by something other than HAV or HBV. However stratifying these donors by the age at time of their jaundice showed that those whose

jaundice occurred after the age of 12, 20.8% lacked evidence of HAV or HBV antibodies compared to only 2% in those whose jaundice occurred up to the age of 12. This meant that if non-A, non-B hepatitis was indeed the cause of jaundice in those individuals lacking HAV or HBV antibodies, then it would seem to be associated with jaundice after the age of 12. During the previous 3 years, 12 cases of overt post-transfusion hepatitis (4 in haemophiliacs who had received imported factor VIII) had occurred in transfusing 400,000 donations. None of the implicated donors in these cases had given a history of jaundice.

28. The PhD study, from 1980-1985, also focused on donors and patients with history of jaundice or hepatitis and came to the same conclusion. Amongst 470 history of jaundice blood donors, almost 90% of these episodes were attributable to HAV, whilst HBV was involved in 4.5% and around 10% had no evidence of HAV or HBV antibodies. Only one of these donors had a grossly elevated SGPT level and high titre coxsackie B4 antibodies were identified (indicating a recent enterovirus infection). (More recent testing of a sample from this donation showed no evidence of HCV infection).

29. Again within the PhD study, testing 1320 patients with a prior history of hepatitis gave a similar figure of 10% lacking HAV or HBV antibodies. A proportion of these samples were tested for SGPT levels and 51 of 619 were found with grossly elevated SGPT levels – and an IEOP test detected 23 positives - 8 due to recent HAV, 6 due to other recent viral infections (HBV, cytomegalovirus (CMV) and Epstein-Barr virus EBV) 2 Rheumatoid Factor positive and 1 Babesia leaving a possible 6 unaccounted for, but possible non-A, non-B hepatitis. Clearly this showed that many of these patients were recovering from a recent rather than a past episode of hepatitis. 35 samples that were known to be HAV and HBV antibody negative were tested for CMV and EBV antibodies and only 3 were negative. This would mean that CMV and EBV infections could possible account for around 90% of those people with a history of jaundice, that lacked both HAV and HBV antibodies, rather than non-A, non-B hepatitis agent(s).

30. In conclusion, exclusion of donors admitting to a history of prior jaundice would have excluded almost 3% of the donor pool at a time when SNBTS was attempting to be self-sufficient. The data linking HBV with a history of jaundice was not

scientifically proven and thus attempting to link non-A, non-B hepatitis with a prior history of jaundice would even now seem implausible especially when it is recognised that non-A, non-B hepatitis has milder ALT elevations than either HAV or HBV.

**Statement of Truth**

I believe that the facts stated in this witness statement are true.

Signed..... *Amelia DL* .....

Dated..... *28 January 2011* .....