PENROSE INQUIRY – C2 – SUMMARY AND QUERIES

Additional Statement

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Summary

- In 1981 Dr McClelland proposed to the MRC working party on Post-Transfusion Hepatitis that a large scale prospective study (along the lines of the US TTV study), including the follow up of recipients, be carried out into post-transfusion NANBH in the UK. His proposal did not receive particular support from the other members of the WP which, in any event, was disbanded in 1981, after its second meeting.
- In 1982/1983 Dr McClelland proposed to the joint BTS working party on Transfusion Associated Hepatitis that a (more modest) prospective study be carried out, again including the follow-up of recipients. It is unclear what happened to this proposal. In any event, the WP met on 27.9.83 (when most of the discussion concerned AIDS) and did not meet again until late 1986.
- In 1984, 1985 and 1986, Drs Dow and Follett reported on their study into surrogate testing. They concluded that post-transfusion NANBH did not appear to be a significant problem in the West of Scotland and that the introduction of surrogate testing was not merited.
- In 1986, in their budget request to the Scottish Office, the SNBTS sought £810k to introduce surrogate testing for NANBH in 1987/88.
- In 1986/87 blood banks in the US introduced surrogate testing.
- The view of the SHHD, DHSS, the English NBTS Directors, and some within SNBTS, was that the introduction of surrogate testing was not justified in the UK without further research.
- In 1986/87 the reconvened BTS working party on Transfusion Associated Hepatitis proposed a multi-centre trial into surrogate markers in donors. Without, in particular, the follow-up of recipients, the scientific value of such a study was limited and the respective Chief Scientific Officer committees in Scotland and England refused to fund the study. In the event, the study proceeded in three English centres (between Sep 1988 and April 1989), with

funding from a policy division of the DHSS, and no Scottish centre was included.

- In March 1987 the SNBTS Directors agreed to recommend to the SHHD that surrogate testing should be implemented from 1.4.88. Professor Cash advised Dr Gunson shortly afterwards that the recommendation should not be taken too seriously and was made with the SNBTS's budget bid in mind.
- In July 1987 the SNBTS Directors wrote to the Lancet that surrogate testing was "irrational, perhaps, but inescapable" because of impending strict liability legislation and the pressure that would arise from the use by commercial fractionators of tested plasma.
- In May 1988 Chiron announced the identification of hepatitis C. Thereafter, the controversy surrounding surrogate testing gradually faded as attention turned to HCV screening.

Queries

(1) Should a large scale prospective study, as originally proposed by Dr McClelland in 1981 (i.e. along the lines of the US TTV and NIH studies and including the follow-up of recipients), have been carried out in the UK in the early 1980s (or at some point thereafter) with the following aims:

(a) to assess the prevalence of post transfusion NANBH in the UK,

(b) to evaluate surrogate markers for the disease,

(c) to investigate the natural progression and seriousness of the disease, and

(d) to produce a library of "known" infected sera with which to evaluate any future assays which became available?

ANSWERS: (1) Yes to all 4 questions.

(2)But there would be advantage in seeking the answers to two further questions: (a) Why did Dr McClelland's 1981 proposal fall? (b) Did the disbanding of the MRC Blood Transfusion Research Committee have anything to do with this? (The answers to these questions may lie in DHSS and SHHD archives and in Minutes of the MRC Systems Board meetings, which I am advised have been retained in the Kew National Archives. Dr Boyd Moir

may also be able to assist as he was medical adviser to SHHD's Chief Scientist Office).

(2) (a) If such a study had been carried out, to what extent is it likely to have met the objectives set out in (1) above? (b) To what extent would such a study have provided more information upon which to base a decision on whether surrogate testing should be introduced?

ANSWERS: (a) I see no reason why a properly resourced and supported UK group could not have achieved parity of performance with the US TTV study group.

(b) I'm not sure what is meant by more information. If DHSS had signalled that it was prepared to consider surrogate testing then the definition of more information would have been donor and patient data derived from a UK population. That said, I always felt that the size of the proposed study (600 patients) may have been rather small to achieve all the objectives described above, notably (c).

(3) (a) Did the conclusions of Drs Dow and Follett[1] place sufficient emphasis on the likely prevalence and seriousness of post-transfusion NANBH? In particular, as well as having regard to reported cases of the disease,(b) did the work of Drs Dow and Follett have sufficient regard to the fact that most cases of NANBH were sub-clinical and were unlikely to be detected without prospective follow-up (by biochemical testing) of recipients?

ANSWERS: (a) No

(b) No, they relied on spontaneous clinical reporting only. This follow up option is notoriously weak, but Dow and Follet seemed aware of this and noted that this may have given them no more than 'the tip of the clinical iceberg'

[1] As contained in Final Report, July 1984 (SGH.002.8040), PhD Thesis, 1985 (LIT.001.3300) and Special Report, May 1986 (SNF.001.1109)

(4) In the second half of the 1980s, (a) Did SHHD medical officers place sufficient weight on the likely prevalence and seriousness of post-transfusion NANBH.[2] (b) To what extent did their views in that regard influence their opinion on whether surrogate testing of blood donors should be introduced?

ANSWERS: (a) I am uncertain how to respond to this question as I have no recollection or record of discussing the topic with SHHD medical staff. That said, the internal SHHD documents supplied by the PI team would indicate fairly clearly that at least one Medical Officer believed that post transfusion NANB was uncommon and of little clinical consequence. He was not alone, but in my view efforts directed towards enhancing what was widely recognised as a very weak evidence base did not enjoy support of all UK Departments of Health, throughout the 1980s.

(b) I defer to former SHHD colleagues, but would suggest their views were largely influenced by opinions in London.

(5) If surrogate testing of blood donors (i.e. testing for elevated ALT and/or anti-HBC) had been introduced in Scotland:

(a) what percentage of donors are likely to have been deferred,

(b) could a sufficient blood supply have been maintained,[3] and

(c) to what extent are cases of post-transfusion hepatitis C likely to have been prevented (having regard, for example, to the finding that in the first six months of HCV screening the prevalence of HCV in Scottish blood donors was 0.088%, and that elevated ALT levels were found in 59% of HCV positive donors)[4]?

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[2] see, for example, the minutes etc by Dr Forrester d.12.6.86 (SGH.002.8142), 26.1.87 (SGH.003.1657), 9.2.87 (SGF.001.2261) and 30.8.88 (SGH.002.4672) and the minute by Dr McIntyre d.6.4.87 (SGH.002.8127)

[3] See, in relation to the question of blood shortages, letter d.28.1.85 from Dr Cash to Dr Bell (SNB.013.4238), letter d.16.1.87 from Dr Cash to Dr Mitchell (SNB.011.3355), the discussion of declining blood collection in Appendix II of PES 1988 (SGH.002.0841 at .0843 to .0849) and letters d.15.1.90, 29.1.90 and 6.2.90 between Professor Cash and Drs Mitchell and Crawford (SNB.013.6496, SNB.014.1589 and SNB.005.2159)

[4] Crawford et al, 1994 (PEN.002.0582)

ANSWERS: **(a) I have always believed that it would have been between 1-3%**

(b) Yes

(c) I believe I judged at the time that the benefit would have been significant, but the costs high and the impact on individual donors and on the robustness of our donor panels had, because we lacked relevant UK data, not been carefully considered.

FOOTNOTE

The briefing papers included by the PI team's package for the C2 topic do not refer to some interesting documents. These can be summarised as follows:

(a) Documents still within Medicines Commission that minute the deliberations of the CSM (Subcommittee on Biological Products) which led members to recommend that product inserts for commercial plasma products imported into the UK could include reference to the increased safety of products whose source plasma had been subject to surrogate testing (1 and 2).

(b) Documents which reveal that the position of the SNBTS Directors on surrogate testing, finally declared in July 1987, whilst at the time subject to much English (and SHHD) ridicule, was, less than 3 years later, espoused by DHSS, CBLA and some former vociferous NBTS Directors. Of interest is that SHHD claimed it had not been briefed by DHSS on much of this radical change in policy. Thus former expressions of righteous indignation and strident calls from SHHD for research before change (which was never supported), rapidly gave way, as predicted by SNBTS Directors, to the inevitable pressures of the market place (3-13). Even more remarkable is the evidence that the introduction of large scale surrogate testing in England and Wales was commenced after the introduction of HCV donation screening - again for market

reasons! The morality of this latter development must surely be addressed in this Inquiry despite the fact that they arose in the period beyond the limits set by the Inquiry Team.

References

1. Letter from JDC to Dr McCelland (SEBTS) dated 4 December 1987 (C5-32)
2. Minute of NBTS RTD meeting dated 20 January 1988, Item 7 (C5-33)
3. Letter from JDC to Dr Donald (CSA) dated 10 March 1989 (C5-34)
4. Letter from JDC to Dr Gunson (NBTS) dated 12 January 1990 (C5-35)
5. Letter from Dr Gunson (NBTS) to JDC dated 16 January 1990 (C5-36)
6. Letter from Mr Hamill (SHHD) to JDC dated 24 January 1990 (C5-37)
7. Letter from JDC to Mr Donald (CSA) dated 25 January 1990 (C5-38)
8. Letter from JDC to Dr Gunson (NBTS) dated 25 January 1990 (C5-39)
9. Letter from Dr Gunson (NBTS) to JDC dated 2 February 1990 (C5-40)
10. Letter from Dr Lane (BPL) to Dr Contreras dated 22 February 1990 (C5-41)
11. Letter from Dr Gunson (NBTS) to JDC dated 14 April 1994 (C5-42)
12. National Blood Authority Report on the NBTS Working Group on ALT Testing dated 1 March 1994 (C5-43)
13. Letter from JDC to Dr Gunson (NBTS) dated 18 April 1994 (C5-44)

Signed

Date