Penrose Inquiry

Availability of tests for the hepatitis C virus and the implementation of screening

Statement (6) by Professor Juhani Leikola

1. The findings on hepatitis C virus were published in spring 1989. Preliminary test kits, manufactured by Ortho, were sent to various blood services and other laboratories in Europe in June.

2. The results of pilot tests were discussed first in Paris at the end of June and then more extensively in Rome in September 1989.

3. The ACVSB convened on 6 November to discuss recent developments in NANB and the new C hepatitis research. Dr. Gunson gave the ACSVB a report on the Rome meeting. "It seemed certain that the anti-HCV test detected viral marker associated with NANB hepatitis" and that routine testing would reduce the incidence of transfusion-transmitted NANB hepatitis. However, there were a number of reservations and questions. The recommendations of the ACTTD were similar.

4. Despite the lack of confirmatory test the Committee supported the general introduction of the Ortho anti-HCV test if the FDA approved it and a pilot study showed it to be feasible and nonproblematic. The pilot study was initiated immediately. It was also felt that the Committee should be developing an economic case for the Department to fund the routine use of the test. The conclusions were by and large the same as we made in Finland. The main difference was that we were not quite as concerned about an official FDA licence. An export permit was, of course, needed.

5. I think the opinion of the Committee was quite reasonable. There were only two conditions for starting the routine screening. Provided these two were fulfilled, the benefits of the screening were such that its introduction to the routine would be warranted.

6. The ACSVB met again in January 1990 to look at the situation. The pilot study had been completed with about 5,000 samples tested. The main problem was the determination of a laboratory cut-off line since there were a number of tests that were not quite positive but not quite negative either. The test should be improved, but overall it seems that the pilot study did not indicate that routine screening would not be feasible. Professor Zuckerman stated at the meeting, that despite the high costs the introduction of screening should not be delayed much beyond approval by the FDA. He also pointed out that the proposed Abbott test would not really be an independent test. It may be noted that both Ortho and Abbott used the same Chiron patent.

7. The Committee reiterated that routine screening should not be introduced in advance of the FDA decision. Some members strongly advocated for testing once this main obstacle had been removed. However, there was no clear recommendation at this meeting that testing should be introduced as soon as the FDA had given green light to the US blood banks. Sci-

entifically, the proposed new screening test did not fulfil all the criteria that had been established for conventional viral screening.

8. In February 1990 the US blood bank organisations recommended to their members that the implementation of the anti-HCV screening should be introduced as soon as possible after the FDA had licensed it. At about the same time Ortho sent to the UK the first generation RIBA test that was to some extent like a confirmatory test. In April the report by Ebeling et al was published in Lancet. The conclusion of the authors was that "the RIBA may offer help in differentiating infective from non-infective blood donors."

9. On 2 May the FDA licensed the Ortho anti-HCV test for use in the US. Two days later Ortho advised that kits were being shipped to US blood centres and screening of the blood supply would commence immediately. This way the main obstacle in the UK considerations was removed and the argument of FDA approval became invalid.

10. The ACVSB met on 24 April, one week before the FDA decision. The reservations as to routine screening had meanwhile grown. The correlation of a positive anti-HCV result to the presence of an infective hepatitis virus might not be quite as good as had been thought. There were serious doubts about the efficacy of the available screening test, and better ones, hopefully, were being developed. As the Chairman summed up the opinion of the participants: "There was inadequate scientific data to support the introduction of the Ortho test for routine screening".

11. The change of attitude of the ACVSB between January and late April 1990 was remarkable. The introduction of an expensive but imperfect test to the routine would not be warranted when better ones were likely to be developed in due course. The US may start screening out of fear of litigations, the French and the Australians have their own reasons and some small European countries may follow suit but the UK should not rush in before a reliable confirmatory test was available and the specificity and sensitivity of the screening test were improved. A large, prospective study was needed for the evaluation of whether of not screening would be suitable for the UK conditions.

12. By the 2 July meeting of the Committee there was evidence especially from the US that anti-HCV did indeed reduce infection incidence and that RIBA was available, not as a good confirmatory test but still as a reasonable supplementary test. The reserved April view of the ACVSB changed again and the Committee returned to the original considerations expressed in the November 1989 and January 1990 meetings. Nevertheless, there was still no rush. Abbott had launched a competing screening test, and it was not known whether it would be better than the Ortho test. The general mood was that screening should be introduced, but it was unclear which test to use and how to apply it in the blood centre routine. It was calculated that a comparative study of the two tests would take approximately four months. The Committee agreed that such an evaluation should be carried out before taking the final decision to commence the anti-HCV screening.

13. To me the decision to carry out the pilot study is understandable since a choice was now available. It could, of course, have been carried out at the same time as implementing the screening with Otho test with which most of the trials had been done. In addition, there was some information that Wellcome would also introduce their own test. The Committee decision may have been a compromise between those favouring fast introduction of the screening and those having scientific reservations as to the quality of the test.

14. However, the Committee underestimated the time needed before the screening test would be really in place. Once the results of the pilot study were ready, their evaluation and interpretation might be complicated since both tests were using the same principle and big differences were not expected. Then it should be agreed on whether the introduction is gradual (like in Finland) or simultaneous in all centres, i.e. the time schedule should then be measured in terms of the slowest one. Practical arrangements needed time. In essence, the outcome of the 2 July meeting meant at least half a year's delay in the introduction of the screening. As it turned out, the time span was more than two times longer. To my understanding only few preparations had been made concerning the practicalities of the large-scale routine testing.

15. The impression I have had from the minutes of the ACVSB meetings from November 1989 to July 1990 is the following. There was first enthusiasm about the new test that seemed to be, at least to some extent, specific for NANB hepatitis and that could prevent a good part of the transfusion-transmitted hepatitis cases. This was something that that had been waited for a long time. Accordingly, once the test had been shown work in practice and the FDA had licensed it, it could and should be introduced also in the UK. What was worrying especially the virological scientists was the method used to develop the test. The virus itself had not been isolated and characterised as conventionally would have been necessary. Therefore, there was no confirmatory test, and an indirect antibody assay recognising a small part of the putative virus had to be used. In spring 1990 the scientific progress was only meagre, although there was preliminary information of some new developments. The wait-and-see attitude became stronger since it would be foolish to rush into the only available, inadequate test when new possibilities were around the corner. There were also questions about the seriousness of the transfusion-transmitted hepatitis C that seemed to be quite often very mild or totally asymptomatic. However, by July 1990 it had become clear that the UK could not postpone this matter forever since the examples of other countries, public health aspects, media coverage, lessons of the HIV epidemic and other non-scientific factors were so pressing that some decision had to be taken, even if reluctantly. The conventional scientific wisdom and virological expertise had to give way to other aspects once there was an established possibility to prevent at least some of the infectious complications of transfusion.

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