# REPORT OF HCV SYMPOSIUM ORGANISED BY ORTHO

## 8TH FEBRUARY 1990

### 1 HCV virus and disease; Professor H Thomas

Reviewed history from Chiron to produce Recombinant antigen. Currently, HCV is thought to be one of the Flavieires related to Yellow Fever, Dengue Fever etc; and which are insect borne.

The Genome has about 10,000 bases and a single ORF.

The Recombinant antigen is thought to represent a nucleocapsiprotein and is still the sole origin of various immunoassays currently in operation. This protein is probably a protease.

Epidemiology. Initial remarks indicate that there is very little HCV in GUM attenders.

"Short incubation" Parenteral NANB hepatitis Virus

Query a further agent - cases numerically low.

Bradley in 1983 (who also supplied Chiron with the original HCV containing material) showed that cases of this nature were associated with a different virus (which was not sensitive to Chloroform) and which was more like a Picorna virus. Filtration characteristics indicated a diameter of 27 nm.

Entheral NANB hepatitis virus

Good epidemiological evidence for a virus in India and North Africa; with clinical characteristics similar to that of hepatitis A but a shorter incubation period. Not associated with chronic disease.

There is also the possibility of sporadic enteral NANB viruses as yet to be identified.

Finally summed up by saying that antibodies to hepatitis C in patients can last for years and there may well be asymptomatic carriers many of whom will have a normal ALT. The virus is "unusual" - ie formerly 'invisible'.

### 2 HCV & The Blood Transfusion Service; Dr J Barbara

i The anti-HCV elisa test takes three hours; not ideal for BTS's.

ii The predictive value in low prevalence populations is low.

iii The validity of the assay appears to be okay (eg haemophiliacs) also, inactivation of FVIII products has been validated by HCV antibody assays in haemophiliacs receiving only heat treated products.

Donor Implications

i How is the virus transmitted?
ii Which donor populations are at risk?

New York blood centre findings appeared to indicate that "viruses hunt in pack" ie donors with low ALT and HBc negative had a low incidence of transmitting HCV whereas donors with a high ALT and high HBc levels had a much greater propensity to transmit HCV. This is not so well reflected in Europe where 71% of anti-HCV positive persons lack surrogate markers.

Predictivity of HCV transmission

The Harvey Alter study (USA) indicated 80% correlation by strict definitions. In Holland Reesinck showed a lower value (50%) using "field criteria".

A recipient study in Holland revealed the following:

Of 226 recipients tested two developed NANB transeminitis. Four had preexisting HCV antibody and four persons were in the process of seroconverting.

He also commented that at least six anti HCV positive donors have not transmitted HCV.

In Japan, where there is a 10-15% of PTH, only 1.5% of people have anti HCV antibodies.

He also made comments about the potential of PCR on cDNA from HCV RNA which might be a better indicatator of infectivity and generation of immunity. Also speculated on the future of assays using structural antigens; and the consequences of the current antigen being non-structural such as the delay to seroconversion and low titres of antibodies.

3 HCV & Haemophiliacs; DR C Lee

A clearly expressed but not very satisfactory talk.

RFH between 1978 and 1983 studied 30 patients with 31 first exposures (query maths).

Of 21 people with haemophilia, all 9 who received commercial concentrates developed anti HCV. 10 of the 12 who received NHS concentrates developed anti-HCV. The two who did not already had anti-HCV.

Of 5 people with FIX deficiency all received NHS concentrates 4 developed HCV but one who also got IgG did not.

Anti-HCV in Haemophiliacs

Those who had well documented NANB were anti-HCV positive and 18 out of 19 such persons were persistently positive.

There is a suggestion that an incubation time to disease and seroconversion in the RFH haemophiliacs was shorter than after a standard transfusion - ? bigger dose. This is taking into account the short term passive transfer of anti-HCV in early factor VIII concentrates. She also suggested that this may be somewhat protected by giving IVIgG or IMIVG.

The trend seems to have stopped since the first generation of heat treated factor VIII.

4 Community Acquired HCV; Dr P Mortimer

Commented that all studies so far have small numbers.

Commented on Dr M Murphy's study reported in a letter in the Lancet at the end of last year describing the leukeamics in Barts Hospital in 3 cohorts between 1983 and 1989 in whom the transmission of HCV appears to have declined. Six patients out of 58 in 1983-84; two patients out of 33 in 1984-86; no patients out of 92 between 1986-89. He pointed out that the platelets given in the first cohort were collected from directed donors. Nevertheless this maybe an indication that the lower incidences of HCV from donors who have applied the self-exclusion criteria for IVDA.

PHLS data show that acute sporadic hepatitis shows anti-HCV in 45 out of 158 NANB; two out of 50 with hepatitis A; and six out of 49 with hepatitis B.

Chronic hepatitis;

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|---|---|
| Cryptogenic | 2 out of 26 patients had anti-HCV antibody. |
| PBC | 0 out of 26. |

Of IVDU, 83 out of 103 are anti-HCV positive.

There is a suggestion that HIV seropositive homosexual men are more likely to be HCV antibody positive (in one study 12 out of 47 comparing with 2 out of 48 seronegative men). Other reports do not form this out.

Mentally handicapped children and adults - 5 out of 90 but not proper controls.

Haemodialysis patients - 1 out of 99 had anti-HCV; this one had had much more blood transfused than the mean of the remaining 28.

In the hospital populations; 100 hospital staff (immediate post needlestick injuries) none had HCV antibody.

Male attenders of STD clinics showed little correlation with the number of sexual partners (two out of 66 with more than 10; four out of 82 with between 6 and 10; one out of 89 with between 3 and 5; and 2 out of 89 with less than 2.

Further Haemophiliac Data

Skidmore from Birmingham reported that there have been no HCV converters receiving Elstree Dry Heat treated factor VIII (19 patients). This study also showed that such concentrates do not transmit Parvovirus. (At question time I mentioned CAL's information on the 5 haemophiliacs in Scotland who have not seroconverted).

Consorts of Haemophiliacs - 10 contacts of 47 HCV Ab positive haemophiliacs were also HCV Ab positive; no consorts of 42 HCV negative haemophiliacs were positive. NB. the consorts are often the administrators of factor VIII concentrates.

5 HCV and the Drug Addict; Dr A Shattock (Dublin)

Note: IVDUs may well have raised ALTs anyway.

In Europe 75% of IVDAs are HCV antibody positive, varying from 30% in Germany to 90% in Spain (Ireland 64%).

HIV seropositivity may (perhaps by a factor of 2) increase HIV seropositivity. He commented that there is a lot of delta infection in Ireland. He also commented that male IVDUs seem not to be very good sexual transmitters (either homo or heterosexually) of HCV.

Anti-HCV levels were independant of age, length of addiction, T4 levels.

He - and also Dr Mortimer - commented on the occasional difficulties in the studies using the Ortho Elisa test on stored samples. Also particularly, heat inactivation appears to produce a lot of false positives using the Ortho Elisa technique.

6 HCV - Some Tropical Studies; Dr C Tibbs

Dr Tibbs emphasised the difficulties of using the Ortho Elisa technique for samples particularly from the tropical areas.

Described three geographical areas - Vanuatu; Zaire; and the Gilbert Islands.

Most of the data he commented on was from the Gilberts; but for Vanuatu up to 6% of men and 5% of women appeared to be seropositive. In Zaire the overall incidence appears to be about 25% with more in women and increase with age.

In the Gilbert Islands there appears to be no difference between age or sex, with an overall incidence of 58%. In institutions it is as high as 87%; and in hospital patients between 78 and 96%. Only two out of 7 expatriate residents were seropositive.

He noted that the Gilbert Islands are hyper-endemic for hepatitis B and delta infection is common; and 11% are HBeAg carriers. There was no correlation of between hepatitis B status and HCV antibody (including delta positive persons).

He gave a preliminary report on work using the Abbott Elisa and the Abbott Bead methods (which use Recombinant peptides from the Genome of the original isolate). The work is very early and difficult to compare but in the Gilbert Islands in 111 people 22 were Abbott Elisa positive compared with 45 Ortho Elisa positive; but only 3 out of the 22 Abbott Elisa positives were positive with the Abbott Peptide Assay.

His final comment was that in the results from topics over estimate the frequency of HCV if one uses the Ortho Elisa and therefore better serology is required.

7 HCV and Liver Cancer; Dr P Johnson

Commented that there is an increasing number of cases of HCC (hepatocellular carcinoma) with no known cirrhosis or other aetology.

Epidemiological evidence from Japan has indicated that HCC has increased from 2% in autopsies in 1963 to 5% in autopsies in 1980. At the same time hepatitis B has decreased and the suggestion is that the increase in HCC is due to more PTH from the 2nd World War onwards.

There are apparently 5 cases of HCC that are associated with PTH.

Initial studies indicate that HCV antibody is widespread among various types of chronic liver disease. This is possibly due to the susceptability of the Ortho Elisa to "stickiness". For example, some of the artifact may be due to total globulin levles being high. Preliminary work with the Abbott assays have failed to confirm the high incidence of the Ortho technique.

For example figures from Italy were quoted as indicating that 38% of cirrhotics with HCC were HCV Ab positive; 21% of serotics alone; this is in spite of 2.2% of HCC without cirrhosis and control figures of 3.9%.

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