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CD4+ AND CD8+ T-CELL COUNTS

Date	CD4+ (/μl)	CD8+ (/μl)	CD4+/CD8+ ratio
Sept 9, 1987	114	282	0·4
Sept 23	284	270	1·05
Jan 8, 1988	125	426	0·29
March 10	245	659	0·37

ds-DNA were 50 U/ml (normal below 25) but fell to normal in the next 2 months. The CD4+ T-cell count was consistently low (table). Delayed-type hypersensitivity skin tests to antigens ('Multitest', Mérieux) and serological tests for cytomegalovirus, Epstein-Barr virus, and hepatitis A and B viruses were negative.

There were no risk factors for HIV infection, and several blood samples tested for HIV by two ELISAs and by western blotting were negative in the following year. Our patient had three infections commonly associated with HIV infection[3] and autoimmune thrombocytopenia, which develops in up to 45% of such patients.[4] This case supports the observation[1,2] that these features and low CD4+ counts are not restricted to HIV infection.

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ANTIBODIES TO HEPATITIS C VIRUS IN HAEMOPHILIA

SIR,—Haemophilic patients are at risk of non-A, non-B hepatitis (NANBH) via plasma derivatives.[1] A fragment of the genome of an NANBH agent designated hepatitis C virus (HCV) has been cloned and an antigenic protein expressed,[2] forming the basis for an immunoassay.[3] We have used this assay to look for IgG antibodies to this protein in samples from 400 French patients with haemophilia, regularly substituted with human clotting factors.

HCV antibody ELISA kits were kindly provided by Ortho Diagnostic Systems, with proficiency and reproducibility panels, which yielded satisfactory results. Frozen plasma samples collected in 1989 and stored at −30°C or less were tested according to the manufacturer's instructions. Results of tests for anti-HCV (and for anti-HIV by western blot) were:

Haemophilia type and severity	*No*	*Anti-HCV+*	*Anti-HIV+*
A; severe	252	166 *(66%)*	176 *(70%)*
A; severe with inhibitor	48	27 *(56%)*	29 *(60%)*
A; moderate	48	31 *(65%)*	9 *(19%)*
B; severe	41	31 *(76%)*	22 *(54%)*
B; moderate	11	8 *(73%)*	4 *(36%)*

Anti-HCV positivity did not appear to be related to the type and severity of haemophilia or to the HIV serological status.

Some patients, heavily transfused with human clotting factor concentrates, were, surprisingly, anti-HCV negative when tested in 1989. To see if antibodies might have disappeared assays were done on serial samples collected yearly between 1985 and 1988 from 39 adult haemophilic patients, 29 anti-HCV negative and 10 anti-HCV positive. They had all been exposed to a similar factor VIII substitution regimen and were selected for being either anti-HIV negative or positive but with limited immunodeficiency (CDC grade 2 or 3 and CD4 lymphocyte count above 200/μl). In 19 of the 29 patients who were anti-HCV negative in 1989 these antibodies had been present in 1985 but disappeared in subsequent samples, in some cases progressively; the remaining 10 patients had been anti-HCV negtive in 1985. All 10 patients positive in 1989 were consistently positive and had acquired antibodies before 1985.

Solvent-detergent treatment with tri-(n-butyl) phosphate and sodium cholate[4,5] is used in France for the viral inactivation of human clotting factor concentrates. On samples from 16 children aged $2\frac{1}{2}$ to 6 years (mean 4) with haemophilia A treated for at least two years with factor VIII concentrate prepared in this way (Biotransfusion) and with no other concentrate, antibodies to HCV were not detected. This confirms the safety of solvent-detergent treatment for factor VIII in respect of the transmission of NANBH.[6]

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SIR,—Preliminary data reported in *The Lancet* of Aug 5 demonstrate that a recently developed test for hepatitis C may detect antibodies (anti-HCV) to the major virus causing post-transfusion non-A, non-B hepatitis (NANBH) in patients receiving blood products derived from donors. We report here the prevalence of anti-HCV in patients with haemophilia who have received blood products manufactured exclusively from blood donors in Scotland by the Scottish National Blood Transfusion Service (SNBTS) and in recipients of commercially prepared factor VIII.

Sera from 61 patients with haemophilia A or B or von Willebrand's disease were tested for anti-HCV (Ortho ELISA). 48 received non-heat-treated factor VIII/IX concentrate (before 1985) and 41 were seropositive; of the 7 who have received only heat-treated concentrates (and a few donations of cryoprecipitate) none were positive; 6 patients received only small amounts of cryoprecipitate or red cells and are all anti-HCV negative (table).

Non-heat-treated concentrates almost inevitably result in NANBH,[1] and in this series 85% (41/48, see table) of patients who will have had a history of NANBH are antibody positive. We do not

ANTI-HCV IN RECIPIENTS OF FACTOR VIII/IX CONCENTRATE

Type of concentrate	Frequency of anti-HCV		
	Non-heat treated (causing NANBH)	Heat-treated	Cryoprecipitate only
Haemophilia A			
SNBTS factor VIII	20/23	0/5	0/2
SNBTS and commercial factor VIII	8/10	0/1	..
Haemophilia B			
SNBTS factor IX	9/10	0/1	..
von Willebrand's disease	4/5	..	0/4
Total	41/48 *(85%)*	0/7	0/6

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know why all such patients are not anti-HCV positive. They have all received many different batches of concentrate, prepared from several thousand individual donations, so all would be expected to be infected since the seroprevalence rate in blood donors is 0·5% or so (Aug 26, p 505). Perhaps they possess antibody but at a level below the detection level of the ELISA—or they may be HCV antigenaemic in the absence of specific antibody.

Of great interest is the finding that all 7 patients who received only heat-treated factor VIII/IX concentrates are anti-HCV negative. This is a potentially valuable observation because hitherto the only way to demonstrate the safety of factor VIII/IX concentrate in respect of NANBH has been to collect blood samples frequently for 6 months after first exposure to concentrate.[2] If our preliminary data are confirmed then a persistently negative anti-HCV test would provide further evidence for the safety of virus-inactivated blood products and one day might obviate the need for frequent liver-function tests, often on small babies.

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SCREENING FOR ANTIBODIES TO ANAESTHETICS

SIR,—Our anaesthetic critics (Aug 12, p 381) should know that this department received 144 requests for laboratory investigation of severe anaphylactoid reactions to general anaesthetics in 1988 and probably twice that number of written and telephoned requests for advice. This year (up to Aug 10) the figure is 102 requests and includes 4 deaths. If translated into the frequency quoted by Dr Noble,[1] these figures would represent all cases expected in the UK—an unlikely situation for any laboratory. The protein reference unit and department of immunology in this hospital has offered an advisory service to anaesthetists for 15 years. We do not solicit investigations, and the fact that the service continues to be used by anaesthetists by choice must mean that the problem is very real. If we have overstated the problem then the epidemiological studies have certainly understated it.

Dr Jones, without detailed knowledge of the Aberdeen case, describes as "absurd the idea of concluding that antibodies found several days after the injection were necessarily present before that injection". The assays were done on samples taken within hours of the patient's collapse and antibodies could not have been formed in such a time interval by an unsensitised patient. While we agree that the presence of antibodies per se is not conclusive proof of involvement in the clinical reaction, would any anaesthetist give suxamethonium to such a patient—any more than he would inject penicillin into a patient with high titre penicillin antibodies?

We were very pleased with the final paragraph of Dr Lunn's letter and would hope that we would be approached by the working group for our opinions since our laboratory and the laboratory of Dr Assem in London are the major centres in the UK with experience of such assays in clinical reactors. The quotation Lunn mentions was taken from the CEPOD report.

There is no reason to think that every surgical patient should be screened. However, patients who have already experienced severe anaphylactoid reactions should certainly be investigated before further surgery. We have encountered a case in which a woman had three cardiac arrests under identical general anaesthesia at three different hospitals before the problem was investigated.

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MANAGEMENT OF ASTHMA IN THE COMMUNITY

SIR,—Your July 22 editorial on management of asthma in the community contains two major flaws. First there is the erroneous statement that Turner-Warwick's survey[1] "documents the disappointingly high frequency of poor control among patients with diagnosed asthma in the community". Second the editorial does not detail the practical issues related to asthma management that are being discussed in general practice.[2]

The results of Turner-Warwick's survey cannot be used to support the cited statement because of the bias in its eligibility criteria towards poorly controlled asthmatic patients. General practitioners were asked to complete questionnaires on ten consecutive patients for whom they prescribed or re-prescribed a bronchodilator aerosol. Patients using their bronchodilator aerosol infrequently were therefore less likely to be included in the survey, and patients maintained solely on inhaled corticosteroids or slow-release aminophylline were not included. Further eligibility criteria were that the patient had to answer in the affirmative to three questions, the first of which was "Have you had symptoms of 'wheezy' breathlessness or chest tightness at anytime during the day or night over the past month?". A negative response would exclude many well-controlled patients from the study, yet no data on the number or type of exclusions were provided. Furthermore, of the 26 000 general practitioners who were asked to take part only 5% responded. This poor response rate led Turner-Warwick to state correctly that "The results do not necessarily reflect the frequency of nocturnal symptoms among all asthmatics in the UK".

The second point we wish to make is your failure to discuss issues currently being debated in general practice with respect to the improvement of asthma management. These issues include the place of asthma mini-clinics, the role of the practice nurse, the advantages and disadvantages of nebulisers, the unavailability of peak expiratory flow meters on National Health Service prescriptions, the effect of the new GP contract[3] on list size and hence time available for chronic disease management, the development of performance review and practice protocols in asthma management, and the acceptance as normal of much chronic asthma morbidity by patients themselves.

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SQUATTING IN SECOND STAGE OF LABOUR

SIR,—We were impressed by Mr Gardosi and colleagues' (July 8, p 74) report of squatting in the second stage of labour—especially by the large sample size and the high proportion (82%) of women who achieved the squatting position. In our own randomised controlled trial[1] evaluating unsupported squatting in the second stage of labour, we had a high non-compliance rate (84%). There are two possible explanations for this difference in compliance rates.

First, the full unsupported squat is a difficult position to maintain for any length of time, and second, our population may be different from that in Milton Keynes. A consumer attitude survey in our hospital[2] showed that although women have considerable interest in alternative birth positions, few are likely to achieve a squatting birth despite much antenatal encouragement and training, possibly because of a lack of motivation of both midwifery staff and participating women during labour.

To determine whether the difference between these two investigations was attributable to the use of the birth cushion or to the attitudes of our staff and women, we have attempted to repeat Gardosi and colleagues' trial. In a pilot study, 13 women were randomised to the cushion arm of the trial (supported squat). Only 3