



Serum neopterin concentrations during acute HIV infection.

At all time-points neopterin, HIV p24 antigen, and HIV antibody (ELISA and western blot) were examined.

an indeterminate pattern on western blot (figure). The diagnosis of HIV infection by conventional western blot (Biotechnologies, Singapore) was confirmed after 3 months. At several time-points before (one serum specimen was occasionally available from an earlier HIV screening programme), during, and after acute HIV infection, serum samples were measured for neopterin (Hennig, Berlin) (figure). In all but one serum the neopterin concentration was above 10 nmol/L. HIV p24 antigen was detectable in only one out of ten samples examined until the positive western blot was observed.

Our observations support the concept that measuring neopterin is a sensitive strategy to detect acute viral syndromes, including acute HIV infection. Neopterin testing seems to have been more informative than p24 testing in the above seroconverter. Moreover, neopterin screening permits exclusion of other infections that could be hazardous to transfusion recipients.

Department of Dermatology and Venereology,  
Central Institute of Blood Transfusion,  
Institute of Hygiene:  
Institute of Medical Chemistry  
and Biochemistry,  
University of Innsbruck,  
Ludwig Boltzmann Institute  
for AIDS Research,  
A-6020 Innsbruck, Austria

ROBERT ZANGERLE  
DIETER SCHÖNITZER  
DIETMAR FUCHS  
JOHANNAS MOST  
MANFRED P. DIERICH  
HELMUT WÄCHTER

1. Alter HJ, Epstein JS, Swenson SG, et al. Prevalence of human immunodeficiency virus type 1 p24 antigen in US blood donors: an assessment of the efficacy of testing in donor screening. *N Engl J Med* 1990; 323: 1312-17.
2. Busch MP, Taylor PE, Leis BA, et al. Screening of selected male blood donors for p24 antigen of human immunodeficiency virus type 1. *N Engl J Med* 1990; 323: 1308-12.
3. Iranz MS, Dudley AW Jr, Luzzo CJ. Case of HIV-1 transmission by antigen-positive, antibody-negative blood. *N Engl J Med* 1991; 325: 1174-75.
4. Hönlinger M, Fuchs D, Hausen A, et al. Serum-Neopterinbestimmung zur zusätzlichen Sicherung der Bluttransfusion. *Deut Med Wochr* 1989; 114: 172-76.
5. Wächter H, Fuchs D, Hausen A, et al. Neopterin: biochemistry—methods—clinical application. Berlin: de Gruyter, 1992.
6. Fendrich C, Luke W, Sahl-Hennig C, et al. Urinary neopterin concentrations in rhesus monkeys after infection with human immunodeficiency virus (SIV<sub>mac</sub>251). *AIDS* 1989; 3: 305-07.

### In-vitro activity of zidovudine against mycoplasma

SIR,—In the past few years several studies have highlighted the potential role for *Mycoplasma fermentans* (incognitus strain) as a cofactor in AIDS pathogenesis.<sup>1,2</sup> Nevertheless, in-vivo confirmation of this hypothesis is still lacking.<sup>2</sup>

We have investigated the association of *M. fermentans* and HIV-1 infection in 93 HIV-positive patients by serological methods and blood cultures with a commercially available non-cellular kit ('Hemofast', International Mycoplasma, Signes, France). Although 12% of patients were seropositive for mycoplasma, only 2 had positive blood cultures, and characterisation of the species

could not be done on subsequent cultivation. Because 39 patients were taking antiretroviral therapy at the time of the study and zidovudine has antibacterial effects,<sup>1</sup> we tested the potential activity of zidovudine against five collection strains of human mycoplasma (*M. pneumoniae*, *M. fermentans*, *M. genitalium*, *M. hominis*, *Ureaplasma urealyticum*) in broth and agar media.<sup>4,5</sup> All species of mycoplasma tested showed a decrease in metabolism (no colour change in broth) with three concentrations of zidovudine (10 µg/ml, 1 µg/ml, 0.1 µg/ml). Furthermore, after inoculation of broth on agar media, we noted substantial loss of mycoplasma concentration compared with control and a modification in the morphological aspects of the colonies in the presence of zidovudine.

These preliminary results demonstrate the inhibitory activity of zidovudine against *Mycoplasma* spp in vitro and raise the possibility that this molecule could act on targets other than reverse transcriptase to influence disease progression in HIV infection. To investigate the presence of mycoplasma in HIV-infected individuals, methods of isolation other than culture should be used in patients taking zidovudine.

ALAIN LAFEUILLE  
GERARD PAPIEROK  
GERARD PAUTRAT  
CLAUDE ESCARGUEL  
PIERRE PELLEGRINO  
ROBERT QUILICHINI

Department of Internal Medicine,  
Chalucet Hospital,  
83000 Toulon, France:  
and International Mycoplasma,  
Signes

1. Montagnier L, Berneman D, Guetard D, et al. Inhibition of HIV prototype strains infectivity by antibodies directed against a peptidic sequence of Mycoplasma. *C R Acad Sci Paris III* 1990; 311: 425-30.
2. Editorial. Mycoplasma and AIDS: what connection? *Lancet* 1991; 337: 20-22.
3. Keith BR, White G, Wilson HR. In vivo efficacy of zidovudine (3'-azido-2'-deoxythymidine) in experimental gram-negative-bacterial infections. *Antimicrob Agents Chemother* 1989; 33: 479-83.
4. Robertson JA, Coppola JE, Heisler OR. Standardized method for determining anti-microbial susceptibility of strains of *Ureaplasma urealyticum* and their response to tetracycline, erythromycin and roxarsolone. *Antimicrob Agents Chemother* 1981; 20: 53-58.
5. Hayes MM, Wear DJ, Lo SC. In vitro anti-microbial susceptibility testing for the newly identified AIDS-associated mycoplasma: *Mycoplasma fermentans* (incognitus strain). *Arch Pathol Lab Med* 1991; 115: 464-66.

### Screening blood donations for HCV

SIR,—Transfusion centres in the UK started routine screening of blood donations for antibody to hepatitis C virus (HCV) on Sept 1, 1991. In the first two months this blood transfusion centre tested 36 843 donations, of which 24 (0.06%) have been confirmed as anti-HCV positive by a second generation radio-immunoblot assay (Ortho Diagnostics); a further 44 (0.12%) were "indeterminate".

24 confirmed seropositive donors (including some of the above 24) have been counselled during this period. 11 (46%) gave a history of intravenous drug use (IVDU) as a single risk factor (2 donors) or in combination with other likely risk factors such as multiple sexual contacts, tattooing, ear-piercing, and blood transfusion. A further 3 donors (1 male, 2 female) gave a history of sexual contact with an IVDU partner. Blood transfusion as a sole factor for HCV infection could be implicated in only 2 donors, 1 of whom had received a massive transfusion from "walk in" donors in Berlin after a post-partum haemorrhage. 3 other donors had a history of transfusion, but 2 of these also admitted to past IVDU. Of those who had a history of multiple sexual partners and/or contact with prostitutes, 3 donors and the sexual partners of 3 others had a history of IVDU. The wife of the other donor in this group had a history of hepatitis B infection but the route of transmission had not been determined. Tattooing was the sole risk factor in 2 donors and ear-piercing alone in 1. In 4 donors no apparent risk factor could be identified.

In this preliminary investigation of our HCV-seropositive donor population, IVDU appears to be the predominant risk factor for transmission of HCV. This finding is consistent with the results of other studies. Archer et al<sup>1</sup> found a history of IVDU in 46% of HCV-positive blood donors in Sydney, and Riestra and Cárcaba<sup>2</sup> found that 80% of drug-using homosexual men in Spain were seropositive, compared with 4.3% of non-drug-using homosexuals.

In our limited study, sexual transmission did not emerge as an important route of transmission of HCV. Indeed, all but 1 donor

who gave a history of sexual contact with multiple partners and/or prostitutes also had a history of IVDU or sexual contact with an IVD user. None of the HCV seropositive donors was homosexual, but since 1983 it has been our policy to deter homosexuals from donating blood. A Spanish study<sup>3</sup> found only 1 female partner of 18 IVD users to be anti-HCV positive, and many other groups have reported that sexual transmission is rare.<sup>4,5</sup>

Exact definition of the routes of transmission of HCV is important, not only for an understanding of the epidemiology and prevention of transmission of HCV but also for policies of donor selection. It is noteworthy that, 8 years after the introduction of "self-exclusion" of potential donors with a history of IVDU, appreciable numbers of donors with a distant history of IVDU are still giving blood because they do not see their past behaviour as relevant to blood contamination today.

As numbers accrue, it might prove informative to compare potential risk factors in donors with indeterminate anti-HCV findings (especially with single C22 bands on radio-immunoblot assay) with those for confirmed positives, to assess the importance of indeterminate reactivity.

We thank Prof R. S. Tedder (University College and Middlesex School of Medicine) for anti-HCV confirmatory work.

S. MACLENNAN  
J. A. BARBARA  
P. HEWITT  
C. MOORE  
M. CONTRERAS

North London Blood Transfusion Centre,  
London NW9 5BG, UK

1. Archer GT, Bivins ML, Kendrick KG, et al. Epidemiology of hepatitis C in blood donors. In: Programme of silver jubilee meeting of Australian Society of Blood Transfusion (Sept 25-28, 1991): 140.
2. Riestra S, Cárdena V. Hepatitis C virus: evidence for sexual transmission. *Br Med J* 1991; 303: 310-11.
3. Esteban JI, Esteban R, Viladomiu L, et al. Hepatitis C virus among risk groups in Spain. *Lancet* 1989; ii: 294-47.
4. Kulho E, Naukkarinen R, Ebeling F, Rasi V, Nikula E, Krusius T. Transmission of hepatitis C virus to sexual partners of seropositive patients with bleeding disorders. *Scand J Infect Dis* (in press).
5. Melbye M, Bisgaard R, Wanzan P, Knudsen K, Ebbesen P, Becker NG. Sexual transmission of HCV: cohort study (1981-9) among European homosexual men. *Br Med J* 1990; 301: 210-12.
6. Tor J, Libre JM, Carbonell M, et al. Sexual transmission of HCV and its relation with HIV and HTLV. *Br Med J* 1990; 301: 1130-33.

### Fetal ductus venosus and its sphincter mechanism

SIR,—Dr Kiserud and colleagues<sup>1</sup> (Dec 7, p 1412) report represents a major advance in fetal medicine. They have used sonic velocimetry with colour-flow mapping to prove the old notion that the ductus venosus provides a direct passage for the oxygenated blood from the umbilical vein directly into the fetal heart and brain without losing oxygen to hepatic tissue.<sup>1</sup>

Their discovery of the jet stream of blood with high-time-averaged maximum velocity, which is directed from the ductus venosus to the foramen ovale, sheds new light on the role of the sphincter mechanism around the origin of the ductus venosus from the umbilical vein. Such a sphincter mechanism was suggested by Amoroso and Barron in 1942, when they discovered bundles of smooth muscle fibres around the origin of the ductus venosus.<sup>2</sup> With angiography, Lind and co-workers<sup>3</sup> showed an indentation or a temporary filling defect in the shadow of the ductus venosus, which supported the presence of a sphincter. In newborn lambs, either injection of noradrenaline or acetylcholine, or stimulation of the severed vagus nerves, always restored the patency of the ductus, which usually closes on the 3rd to 6th day of age.<sup>3</sup> With histochemical techniques we have found an accumulation of adrenergic nerve fibres, concomitant with a thickening of the vessel wall, at the origin of the ductus venosus.<sup>4</sup> Additionally, in specimens of human ductus venosus obtained at 21-23 weeks of gestation we have observed a contractile response in this region to noradrenaline (blocked by phenoxybenzamine), acetylcholine, and 5-HT.<sup>5</sup>

Kiserud and colleagues<sup>1</sup> work has altered the view about the function of a sphincter in the ductus venosus. Formerly, the function was thought to be protection of the fetal heart against a sudden large increase in venous return—eg, in a uterine contraction. It now seems that the sphincter also serves to regulate the resistance

to blood flow in the vessel, in order to maintain the jet stream into the foramen ovale to provide optimum oxygenation to the fetal brain. The maintenance of a sufficient venous return of well-oxygenated blood to the left side of the fetal heart might in some situations have to be supported by pharmacological intervention, stimulating the contraction of the sphincter, and can possibly be included in consideration of a fetal therapy.

Department of Obstetrics and Gynaecology,  
Karolinska Institutet,  
Danderyd Hospital,  
S-182 88 Danderyd, Sweden

GERHARD GENNSER

1. Barclay AE, Franklin KJ, Prichard MM. The foetal circulation and cardiovascular system, and the changes that they undergo at birth. Oxford: Blackwell Scientific Publications, 1944.
2. Lind J, Stern L, Wegelius C. Human foetal and neonatal circulation. Springfield, Ill: Charles C. Thomas, 1964.
3. Peltonen T, Hirvonen L. Experimental studies on fetal and neonatal circulation. *Acta Paediatr Scand* 1965; suppl 161: 1-55.
4. Gennser G, Öwman C, Sjöberg N-O. Histochemical evidence of an amineergic sphincter mechanism in the ductus venosus of the human foetus. In: Horsky J, Stembera ZK, eds. Intra-uterine dangers to the foetus. Amsterdam: Excerpta Medica Foundation, 1967: 180-81.
5. Ehinger B, Gennser G, Öwman C, Persson H, Sjöberg N-O. Histochemical and pharmacological studies on amine mechanisms in the umbilical cord, umbilical vein and ductus venosus of the human foetus. *Acta Physiol Scand* 1968; 72: 15-24.

### Treatment strategies for Alzheimer's disease

SIR,—Deposition of  $\beta$ -amyloid protein, as, for example, Dr Roberts and colleagues report (Dec 7, p 1422), has provided the basis for many studies aimed at treatment of Alzheimer's disease (AD) by slowing progression of pathological changes.<sup>1</sup> Even if this line of research eventually leads to new treatment, drugs that affect neurotransmission will still be needed in most patients to rescue functional activities that are already lost as well as in all patients during development of the alternative treatment.

The transmitter neurochemistry of living AD patients has been described—eg, relative sparing of dopamine,  $\gamma$ -aminobutyric acid, and somatostatin, as well as noradrenaline—and the critically affected neocortical neurons were thought to be corticocortical glutamatergic pyramidal cells, in particular those in parietotemporal areas. Thus some of us proposed<sup>2</sup> that the glutamate partial agonist, D-cycloserine, should be tested for clinical efficacy. Although this compound should promote the effect on the N-methyl-D-aspartate receptor complex of the remaining pool of transmitter glutamate it is unlikely to affect responses of other subtypes of glutamate receptor. A new class of drug, the selective serotonin (5-HT) 1A receptor antagonist,<sup>3,4</sup> should promote all effects of the remaining glutamate transmitter pool by inhibiting the tonic hyperpolarising action of endogenous 5-HT on pyramidal neurons,<sup>5</sup> thereby compensating for reduced excitatory (glutamatergic) input caused by the degenerative process. The approach is also indicated since the 1A receptor seems enriched on the appropriate cell—neocortical pyramidal neurons<sup>6</sup> of human superficial layers (table). Furthermore, even in post-mortem AD brain, half the many cortical areas assayed had no evidence of a selective reduction in presynaptic 5-HT activity.<sup>7</sup> AD is slowly progressive, so this deficiency is probably never widespread, a feature consistent with the 5-hydroxyindoleacetic acid (5-HIAA) concentration of ventricular cerebrospinal fluid (CSF) in AD patients which was not lower than that in controls (our unpublished data; samples as described in ref 7). Indeed those 5-HT nerve endings remaining seem most active in the most demented patients.

#### 5-HT<sub>1A</sub> RECEPTORS IN HUMAN AND RAT NEOCORTEX

Cortical layers	B <sub>max</sub> (fmol/mg frontal cortex tissue)*	
	Human (n = 7)	Rat (n = 5)
Superficial	73 (6)†	28 (2)
Deep	27 (1)	37 (3)

\*Mean (SEM) by autoradiography with [<sup>3</sup>H]-8-OH-DPAT (8 concentrations, 0.5-5 nmol/l).

†Significantly higher (p < 0.005, Student's t-test) than all other values. Human samples were from neurosurgical craniotomies of adult non-demented patients. Note highest binding in human superficial layers: by comparison with adjacent histological sections (not shown) this region of the autoradiograph corresponded mainly to layer II.