

	Mean (SD) <i>E coli</i> (\log_{10}) per liver		
	3 h	48 h	72 h
Albumin	3.6 (0.2)	4.5 (0.10)	4.8 (0.01)
PolyHbX1	3.5 (0.1)	4.5 (0.06)	4.8 (0.05)

Table: Proliferation of *E coli* 018 K1 in livers of CBA/J mice

intravenous dose of a modified haemoglobin solution. They strongly suggested that modified haemoglobin solutions should not be used as blood substitutes in view of the risk of fulminating sepsis. We have carried out a similar study with a completely different outcome. A polymerised human haemoglobin solution (polyHbX1, developed at the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service) was tested in a mouse infection model (12 animals) at a single intravenous dose of 15 mL/kg. An equivalent dose of human albumin solution served as control (12 animals). 8×10^3 *E coli* 018 K1 (gift from E Griffiths) was inoculated intravenously 1 h after the test solution, and the number of viable organisms in several organs was measured (table). No difference was found in bacterial numbers between polyHbX1-treated and control mice and all animals survived. The sensitivity of a comparable infection model in response to various modifiers has been shown previously.³

The discrepancy between our findings and those of Griffiths et al may be due to differences between the haemoglobin solutions in purity, or stability of tissue distribution, to the use of different mouse strains, or to the different sites of inoculation of *E coli*. We find it puzzling that such a small difference in experimental design should have such a striking impact on outcome. Further study is needed to find out whether an increase in susceptibility to bacterial infections is a real hazard of haemoglobin-based blood substitutes.

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Subcutaneous immunoglobulin replacement in patients with primary antibody deficiencies

SIR—Gardulf et al (Feb 11, p 365) report that subcutaneous immunoglobulin (IgG) administration is a safe and convenient method for substitution in hypogammaglobulinaemic patients. We agree that adequate serum IgG concentrations can be achieved in compliant patients.^{1,2} We have found, however, that in many patients compliance with home treatment decreases (as shown by serum IgG concentrations <3 g/L), mainly because of pronounced and recurrent soreness at the site of infusion. This side-effect seems to be associated with certain batches of the 16% immunoglobulin preparations, possibly related to prekallikrein activator,³ and is not patient dependent. We have gradually switched to intravenous administration, and since 1990 this has been the method used in most of our patients. Patients seem to prefer intravenous substitution to the subcutaneous method. To decrease costs and

inconvenience, we aim at administration at home or at the surgery of the general practitioner. Of the 31 adult patients (12 women, 19 men, mean age 42, range 18-79 years) with hypogammaglobulinaemia at our outpatient clinic, 29 receive IgG substitution intravenously, 7 of them receive infusions at home (mainly given by a partner), and 11 at the general practitioner's surgery. 1 patient uses IgG subcutaneously and 1 intramuscularly. The patients report occasional mild systemic reactions (fever, chills, headache), but no severe reactions have been noted.

The yearly costs of the immunoglobulin preparations, based on an average of 18 g per 4 weeks, are about US \$5380 for subcutaneous treatment (syringe driver not included) compared with \$9530 for intravenous treatment—a smaller difference than in the Scandinavian study.

The indications for subcutaneous treatment in our setting for adults are limited to side-effects on intravenous therapy and poor venous access. In children, the subcutaneous route is often preferred.

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Increased urinary dipeptidyl peptidase IV activity in extrahepatic biliary atresia

SIR—Extrahepatic biliary atresia (EHBA) occurs in 1 in 10 000 to 1 in 20 000 live births. Survival of patients with EHBA increased substantially after the description of portoenterostomy by Kasai et al.¹ Successful re-establishment of bile flow and long-term survival after a Kasai operation depends on the age at the time of surgery.²⁻⁴ Patients who cannot be treated with a Kasai procedure or who redevelop symptoms of hepatic failure due to the long-term consequences of recurring cholestasis are treated with liver transplantation, an operation not available in some countries. In Japan, a programme has been developed to inform parents of patients to routinely watch for signs of cholestasis (white stool) and immediately seek help. It was hoped that this strategy would lead to earlier diagnosis of EHBA and to timely Kasai operations. However, recent evaluation of the programme did not show improvement in the age of patients at the time of Kasai surgery,⁵ strongly indicating that a specific and easy-to-perform test is necessary for early diagnosis of EHBA.

We tested the proteolytic enzyme, dipeptidyl peptidase IV (DPPIV), also known as CD26, in the urine of control and EHBA patients. DPPIV is present on the brush border of the bile canaliculi, renal tubules, and gut epithelium and on the surface of some haemopoietic and T-lineage cells. Urine samples were collected from 35 healthy individuals at 2-8 weeks of age and from 4 EHBA patients (6-8 weeks). Urine samples of 2 EHBA patients were analysed at different time points before Kasai surgery. All patients were jaundiced at the time of DPPIV measurements. EHBA was diagnosed by