tion seems to be increased in people who are also infected with hepatitis B virus (HBV) or HCV [3].

Serum specimens from 20 HBsAg-negative and anti-HIV-negative end-stage renal disease (ESRD) patients were tested for HGV RNA: 16 patients were on haemodialysis (HD) and four were on continuous ambulatory peritoneal dialysis (CAPD) treatment. In the HD group, 14 patients were anti-HCV reactive (positive or indeterminate cases) by third-generation assays and, among these, all but two were HCV RNA positive: six with genotype 1b and six with genotype 2. In the CAPD group, three of four patients were both anti-HCV reactive and HCV RNA positive: two with genotype 1b and one with genotype 2.

HGV RNA was detected by reverse transcription polymerase chain reaction (RT-PCR) amplification with multiple non-overlapping nested primer sets from 5' UTR, NS3 (helicase), NS5a and NS5b (polymerase) regions of the virus.

On the whole, three of 20 (15%) uremic patients had detectable HGV viraemia by PCR: all three belonged to the HD group and none to the CAPD group. This frequency is higher than the 10% found among an ESRD cohort of patients in Japan [5]. In our three positive subjects, two patients were anti-HCV positive/HCV RNA positive and one was anti-HCV negative/HCV RNA positive, but with occasionally raised serum transaminase levels.

In conclusion, our data suggest that HGV infection may be present in a proportion of patients with or without HCV infection and, moreover, that in HBV-negative/HCV-negative individuals on regular replacement therapy with even sporadic elevation of ALT/AST level it may be useful to investigate on the presence of novel hepatotropic agents such as HGV. The clinical significance of this new virus as a cause of acute or chronic liver disease in the dialysis population remains to be determined by extensive epidemiological studies.

Elevated pentosidine content in amyloid deposits and in insoluble amyloid fibrils from patients with β2-microglobulin amyloidosis

Sir,

Advanced glycation end products (AGEPs) are formed from the non-enzymatic cross-linking of proteins with sugars. AGEPs may form on any protein (haemoglobin, albumin and tissue proteins) and accumulate normally with ageing or pathologically as in diabetes and renal failure [1]. Recently, AGEP-modified β2-microglobulin has been incriminated in the pathogenesis of dialysis-related amyloidosis [2]. The presence of AGEPs results in a decrease in the pI of β2-microglobulin (normally 5.7 and 5.3) forming the more acidic species thought to be specific for dialysis-related amyloidosis [2].

We have found that the most acidic isomers of β2-microglobulin are not specific for amyloidosis nor for renal failure [3]. We therefore wanted to measure the AGE content of the surgical specimens of carpal tunnel from patients having β2-microglobulin amyloidosis, and compare these concentrations to previously studied serum and tissue levels from patients with renal failure on dialysis. Also, we wanted to establish whether the most insoluble amyloid fibrils are enriched with AGEPs, a finding which would be predicted by the hypothesis that AGEP-modified β2-microglobulin plays a key role in dialysis-related amyloidosis.

Five amyloid deposits were obtained surgically from the carpal tunnels of four haemodialysis patients with histologically proven β2-microglobulin amyloidosis. Each deposit was submitted to amyloid fibril purification procedure as previously reported [3], until the HCl guanidine 6M solution step. The content of the long-lived AGEP compound, pentosidine, was determined in the samples as previously reported [4], both in the prepurified amyloid fibrils as well as in the aliquots of untreated surgical specimens.

The results are presented in Fig. 1. The crude surgical specimens contained a mean of 232 ± 34 pmol/mg protein of pentosidine, while the amyloid fibril-enriched counterparts contained 132 ± 39 pmol/mg protein.

These analyses show that carpal tissue from amyloidotic patients has a strikingly increased AGE content—an 10-fold the serum concentration, 4-fold the skin and 2-fold the peritoneal tissue content of pentosidine previously observed in dialysis patients [4]. However, after purification, no increase was seen in AGE content of the amyloid fibrils. Thus the bulk of AGEs are not strongly trapped in the amyloid fibrils, but may be distributed throughout the amyloid deposits. Although not forming part of the core of amyloid fibrils, AGEs might play a role in the predilection of β2-microglobulin amyloidosis for tendons, synovia and bones. This observation deserves further study.
using ultrastructural techniques and immunolocalization of the AGEPs within the amyloid.

LP 9008 CNRS and Unit 249 INSERM, Centre de Recherches en Biochimie Macromoléculaire, 1919, Route de Mende BP5051, 34033 Montpellier Cedex, France
*Department of Nephrology, University Hospitals of Cleveland, 11100 Euclid Avenue, Cleveland, OH 44106-5048, USA
†Department of Nephrology, University Hospital 'Lapeyronie', 34059 Montpellier Cedex, France


Pre-operative autologous blood donation in haemodialysis patients

Sir,

Due to attendant risks of homologous blood transfusions, including alloimmunization, transmission of blood-borne infections and transfusion reactions, autologous blood donation has emerged as a logical alternative. The use of r-HuEPO has been consistently shown to facilitate the presurgical collection of autologous blood, so that autologous transfusion has become a standard therapy in healthy subjects including alloimmunization, transmission of blood-borne infections and transfusion reactions, autologous blood donation has emerged as a logical alternative. The use of r-HuEPO has been consistently shown to facilitate the presurgical collection of autologous blood, so that autologous transfusion has become a standard therapy in healthy subjects undergoing elective surgery [1-3]. However, there is paucity of bibliographic data [4] concerning pre-operative autologous blood donation in haemodialysis patients. Is it feasible? We are reporting on our experience gained with a haemodialysis patient, who successfully autodonated 3 units of blood prior to elective hip replacement.

A 73-year-old female, weight 73 kg, who had been on haemodialysis since October 1988, had to undergo total left hip arthroplasty, due to severe osteoarthritis causing her intractable joint pain during the night. The patient approved blood autodonation as a part of her treatment and an informed consent was obtained.

For the past 30 months her anaemia had been treated with r-HuEPO and iron supplements, given intravenously at the end of haemodialysis. Aiming at maintaining a haematocrit of about 34-37%, the mean maintenance dose of the r-HuEPO had consistently been 60 (50-70) IU/week, whereas iron dosing was dictated by serum ferritin. On the 25th pre-operative day, haematocrit, ferritin and transferrin saturation were 36.9%, 300 μg/l and 25%, respectively. Based on those data, and considering the published experience [1-3] with autologous blood phlebotomy in the elective surgery setting, we opted to collect 900–1100 ml autologous blood during the 2-week period before surgery. To facilitate this, we empirically increased the dose of r-HuEPO from 55 to 500 IU/kg/week, starting on the 21st pre-operative day, in an attempt to intensify the erythropoietic response. To monitor the patient's blood volume status during the peri-operative period, haematocrit was measured from predialysis blood samples, drawn on each haemodialysis session, 2 weeks pre-operatively and 1 week post-operatively (Fig. 1). The patient received three consecutive phlebotomies, before the beginning of haemodialysis, on the 15th, 8th and 3rd pre-operative days and during each phlebotomy 350 ml of autologous donated blood was taken. The blood was collected in plastic bags containing CPDA 1 and stored at 4-6°C as packed red blood cells. Pre-phlebotomy haematocrit remained on all occasions greater than 34%. The patient tolerated all phlebotomies well and no adverse events were noted. She was hospitalized on schedule for hip surgery. At operation, she was transfused with 3 units of autologous packed red blood cells. Her clinical condition remained stable during surgery and no additional homologous blood transfusions were required. Haematocrit, which was 35.5% just before surgery, decreased to 32.5% and 28.5% on the 1st and 2nd post-operative days, respectively, and then increased to 30.7% on the 6th post-operative day (Fig. 1). On that day r-HuEPO dose was decreased to 55 IU/kg/week. On the 13th post-operative day her haematocrit was 35.2%. Her hospitalization was totally uneventful and she was discharged on the 9th post-operative day.

The cumulative autologous red cell volume procured in our patient was 384 ml, calculated from the volume and the haematocrit of the individual collections, and it was relatively comparable to that generated with r-HuEPO treatment in non-uraemic patients undergoing elective surgery [1,2]. The 9-fold increase of r-HuEPO 3 weeks prior to surgery contributed largely to the donation success and did not permit any further lowering of the haematocrit during the peri-operative period. However, it is unclear if the yield of blood autodonation could have been at least the same if our patient had remained on her maintenance r-HuEPO dose throughout the whole donation phase, and the three phlebotomies were equally spaced within the 6-week period prior to surgery, given that liquid blood can be stored for up to 42 days. Timing of blood autodonation, number of donating units that can be procured pre-operatively and optimal r-HuEPO dose for maximal peri-operative erythropoiesis merit further study in the haemodialysis setting.

Fig. 1. Haematocrit changes during the peri-operative period.