Letters and replies

About familial interstitial nephritis and retinitis pigmentosa

Sir,
We read with great interest the case reported by Farrel et al. concerning the unusual association of familial interstitial nephritis and retinitis pigmentosa [1]. We completely agree with their conclusions and would like to note that apart the medullary cystic disease and the Bardet-Biedl syndrome, there is at least one other rare disease that associates interstitial nephritis and retinitis pigmentosa. The cranioectodermal dysplasia described in 1975 by Sensenbrenner and known as Sensenbrenner’s syndrome consists of dolichocephaly, sparse slow growing hair, epicanthal folds, hypodontia or microdontia, short span, brachydactyly and brachyphodia and a narrow thorax [2]. This affection has an autosomic recessive mode of inheritance. Intelligence is reputed to be normal. Eke et al. recently reported the occurrence of retinitis pigmentosa in these patients [3]. Savill et al. wondered if poor renal outcome with evolution towards end-stage renal failure (ESRF) was part of the disease [4]. Among the 12 reported cases in the literature, seven at least presented poor outcome and evolution to ESRF.

We recently reported the case of a young girl with the characteristic of the Sensenbrenner syndrome who underwent ESRF and received successfully a cadaveric-donor renal transplant [5]. Renal histology was consistant with nephronophtisis. In order to clarify the renal involvement in this syndrome, we tested the NPHE1 nephrophtisis associated locus in our patient and found that the nephrophtisis-implicated deletion was not present [5,6]. If the absence of deletion of the NPHE1 gene is confirmed in other patients with the Sensenbrenner syndrome, the renal involvement will be considered as part of the syndrome. Taken together, these assertions are consistent with the existence of several associations implicating retinitis pigmentosa and interstitial nephritis.

Thus, Sensenbrenner syndrome, as well as nephrophtisis, Bardet-Biedl syndrome, and the patients presented by Farrell et al., although sharing a comparable phenotype, seem to have a different genetic basis.

Sir,
In his letter Dr Tsimaratos interestingly draws attention to other cases in which there is occurrence of retinitis pigmentosa in association with end-stage renal failure. In particular he alludes to Sensenbrenner’s syndrome [1]. Neither of the two patients described in our case report fulfil the criteria for this syndrome or the variant described by Dr Tsimaratos. The renal lesion in our cases was an interstitial nephritis rather than nephrophtisis.

We do agree with him that Sensenbrenner’s syndrome, Bardet-Biedl syndrome and the patients described in our case report share certain characteristics. It would appear that ultimately like many other rare syndromes, the only correct method of classifying these cases will be based on knowledge of the underlying genetic abnormality rather than into syndromes based solely on clinical symptoms and physical findings.

Replay

Sir,

In his letter Dr Tsimaratos interestingly draws attention to other cases in which there is occurrence of retinitis pigmentosa in association with end-stage renal failure. In particular he alludes to Sensenbrenner’s syndrome [1]. Neither of the two patients described in our case report fulfil the criteria for this syndrome or the variant described by Dr Tsimaratos. The renal lesion in our cases was an interstitial nephritis rather than nephrophtisis.

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Is ultrasound guided cannulation of the internal jugular vein really superior to landmark techniques?

Sir,

Farrell and Gellens [1] conclude, from their retrospective study, that the ultrasound guided cannulation of the internal jugular vein is superior to the landmark technique in success rate and morbidity. The authors support their thesis by poor results in the landmark group (successful cannulations, 82%; 35.9% successful first attempt, 35.9%; arterial puncture, 7.7%) and refer to other prospective, randomized studies with ‘similar results’ [2,3].

Reviewing our own experience and some large studies (Table 1), we found that the landmark techniques for internal jugular catheterization were obviously more effective before the introduction of ultrasound guidance, and the incidence of inadvertent arterial puncture was remarkably lower. Accordingly, Senef reports success rates of 90–99%, usually within the first three attempts, for elective insertions [4].

These results raise a number of questions. Is ultrasound guidance really superior with respect to these ‘historical controls’? Has the increasing use of ultrasound for central venous catheterization led to less experience and training in landmark techniques? Do physicians who favour the ultra-
### Table 1. Efficacy of the landmark-based cannulation of the internal jugular vein

<table>
<thead>
<tr>
<th>Authors [Ref.]</th>
<th>Number of patients or cannulation attempts</th>
<th>Overall success rate (%)</th>
<th>Successful first attempt (%)</th>
<th>Arterial puncture (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farrell et al. [1]ᵃ</td>
<td>39</td>
<td>82.0</td>
<td>35.9</td>
<td>7.7</td>
</tr>
<tr>
<td>English et al. [5]</td>
<td>500</td>
<td>94.8</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>Khatri et al. [6]ᵇ</td>
<td>320</td>
<td>91</td>
<td>85.4</td>
<td>?</td>
</tr>
<tr>
<td>Messahel et al. [7]</td>
<td>335</td>
<td>100</td>
<td>94</td>
<td>1</td>
</tr>
<tr>
<td>Rao et al. [8]ᶜ</td>
<td>316</td>
<td>98</td>
<td>94</td>
<td>1</td>
</tr>
<tr>
<td>Szajdjer et al. [9]ᵈ</td>
<td>453</td>
<td>83.4</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td>Sharrock et al. [10]</td>
<td>212</td>
<td>99</td>
<td>82.5</td>
<td>1.4</td>
</tr>
<tr>
<td>Oda et al. [11]ᶜ</td>
<td>456</td>
<td>95.8</td>
<td>1.1</td>
<td></td>
</tr>
</tbody>
</table>

ᵃLandmark group only.  
ᵇIncluding dialysis catheters and pulmonary artery catheters.  
ᶜIncluding neonates and infants.  
ᵈ48% of cannulations by inexperienced physicians under teaching supervision.

Sound guided technique choose the adequate landmarks and techniques in their comparative groups? Ultrasound assistance may be helpful in particular cases, however, for clinical routine practice we agree with Seneff: ‘Ultrasound localization to aid internal jugular vein catheterization is unnecessary for a procedure that already has a high success rate’ [4].

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**Reply**

Sir,

In reply to the letter of Dr Muhm, I would like to make the following points.

(i) The majority of previous studies, including many quoted in your letter, have involved internal jugular cannulation by anaesthetists in patients undergoing surgery or in intensive care requiring invasive monitoring [1–3]. These groups greatly differ from haemodialysis patients in that it is frequently the first cannulation of the jugular vein. Unfortunately this is rarely the case in haemodialysis patients requiring access. One of the major advantages of ultrasound in the haemodialysis group is the ability to visualize the anatomy of the vein and whether it is thrombosed or not prior to attempted cannulation. Obviously no matter how good an individual is at the landmark technique, it is not possible for them to know prior to the procedure whether the internal jugular vein is thrombosed or not.

(ii) I agree that it is likely that the use of ultrasound has led to operators less experienced at the landmark technique.

In my opinion, one should use the advances in visualization techniques available. Our study demonstrates a 0% arterial puncture rate with a very high first time successful cannulation rate [4]. This translates directly into a safer and less painful procedure for the patient which should be the ultimate goal for all invasive techniques. Refusing to use ultrasound is like driving a car without a safety belt—it can be done safely most of the time but the price of not using it may be high.

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Outcome of renal transplantation in Wiskott-Aldrich syndrome

Sir,

We were interested to read the recent article of Fischer et al. regarding the fatal outcome of a renal transplant in a patient with Wiskott-Aldrich syndrome [1]. In 1993, we reported the first case of renal transplantation in this condition [2] and would like to offer some comment and follow-up.

In the case reported, the recipient died 3 months after transplantation following a number of infective complications including CMV, bacterial sepsis, herpes zoster and Pneumocystis carinii pneumonia. Lymphoproliferative disease was also detected shortly before death. As the authors note, it is difficult to ignore the conclusion that the burden of immunosuppression given was excessive. In our patient, we avoided the use of antibody therapy. We also used a reduced dose of azathioprine (1 mg/kg rather than 2 mg/kg) and aimed for a lower trough cyclosporin level (100–150 ng/ml rather than 200–250 ng/ml).

In contrast to our experience, their patient (and a second patient reported in the French literature [3]) required treatment for rejection, including with anti-thymocyte globulin. It is instructive to note that the defects in cellular immunity that characterize this condition do not prevent rejection. However, given the predisposition of such patients to infection and lymphoproliferative disease, we would urge caution in the aggressive treatment of such events. It may be better to concede graft function than to risk over-immunosuppression. In particular, we would not have treated with pulses of methylprednisolone without biopsy proof of rejection.

What can we conclude? If such patients are to be transplanted successfully, it seems critical to reduce their overall immunosuppressive burden. Good tissue matching may be important in this respect; our patient received a 011 ABDR mismatched kidney. Our patient had received no blood transfusions in the 10 years prior to his transplant, and at the time of transplantation had a 0% panel reactivity and negative FACS analysis, indicating minimal immunological activation. It may also have been relevant that the donor organs were in good condition with a short cold ischaemic time, and that there was immediate graft function. Avoidance of a CMV positive donor may in future be appropriate.

One last word of caution. Despite an uncomplicated post-transplant course, our patient died at home 35 months after Kantonsspital transplantation and no evidence of rejection. transplant and no evidence of lymphoma. This unfortunate outcome, probably acceptable. We also agree with Dr Andrews and Dr Kohman’s recommendations to minimize the risk of acute rejection by carefully selecting a donor with good HLA matching and a short cold ischaemia time. Our patient received a one-haplotype-matched kidney from his father and despite the defect in cellular immunity associated with WAS he developed rapidly aggressive rejection episodes. We were very interested to receive follow-up information about the first WAS renal transplant recipient reported in the literature [3] who died at age 49, nearly 3 years after transplantation, of presumed cardiac cause (severe triple vessel coronary artery disease), with a perfectly functioning kidney function (creatinine 99 μmol/l at the time of death), it remains to be seen whether the long-term prognosis of transplantation in Wiskott-Aldrich syndrome is sufficient to justify initial enthusiasm, and this will need to be borne in mind when considering future candidates for transplantation and the appropriateness of organ allocation.

Reply

Sir,

We thank Dr Andrews and Dr Kohman for their comments on our case report of renal transplantation in a patient with Wiskott-Aldrich syndrome (WAS) [1] and completely agree with their recommendations to reduce the dose of immunosuppressive drugs, and especially to avoid the use of anti-thymocyte globulin should a rejection episode occur. As pulses of methylprednisolone were well tolerated in the case described by Meisels et al. [2] the cautious use of steroids for treatment of a well documented rejection episode is probably acceptable. We also agree with Dr Andrews and Dr Kohman’s recommendations to minimize the risk of acute rejection by carefully selecting a donor with good HLA matching and a short cold ischaemia time. Our patient received a one-haplotype-matched kidney from his father and despite the defect in cellular immunity associated with WAS he developed rapidly aggressive rejection episodes. We were very interested to receive follow-up information about the first WAS renal transplant recipient reported in the literature [3] who died at age 49, nearly 3 years after transplantation, of presumed cardiac cause (severe triple vessel coronary artery disease), with a perfectly functioning transplant and no evidence of lymphoma. This unfortunate outcome, probably unrelated to underlying WAS, interestingly shows that patients with WAS may tolerate chronic immunosuppressive therapy without developing malignancy. We finally agree that, given the reduced life expectancy of patients with WAS, the appropriateness of organ allocation is a critical issue in the decision whether to accept such patients as candidates for transplantation. In our opinion only WAS patients with poor tolerance of their renal replacement therapy, willing to accept the increased risk of immunosuppression-related complications and having a potential living-related donor should be considered for transplantation.

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transplantation in Wiskott-Aldrich syndrome. Transplantation 1993; 56: 747–748

Comments of a frustrated Batavian friend having unsuccessfully practised Yoga to solve the Nephroquiz

Although I do not consider myself a beginner, I was unable to solve the Nephroquiz ‘Out of the Blue’ in the issue of last September. I have studied Figure 1 for quite a long time. Most puzzling to me was the question of whether the extremity presented was the right leg of a supine patient or the left arm of a prone patient. In either case the two severely cyanotic fingertips in the picture most probably belonged to a second individual who was also seriously ill. When I tried to simulate the position of the fingers by lying on my back or on my stomach, the only thing I accomplished was that I almost twisted first my left and subsequently my right arm.

In addition to this acrobatic exercise the presented case raised another question, which is usually the first that I ask in such instances: ‘Who examined the urinary sediment?’ First, there is a failure to report on the morphology of the erythrocytes. I can imagine that the authors left this out to make their question not too easy. But I certainly refuse to believe that there were no erythrocyte casts present. In such a case of active IgA nephropathy the absence of erythrocyte casts must be considered as highly unusual. Such a result is most often caused by the failure of the examiner to screen the sediment carefully at low magnification (×100). We have shown in a blinded, controlled study of 107 patients with proven causes of either glomerular or non-glomerular haematuria that, in the patients with glomerular haematuria, erythrocyte casts can be detected in 83% of the cases [1]. Especially the presence of dysmorphic erythrocytes should be a reason for a thorough screening of the entire sediment. This may take some time (up to 10 min), but the examiner is often rewarded by the detection of one or two characteristic erythrocyte casts.

We have recently proposed a very simple procedure to fix the urinary sediment [2]. It will enable the beginner to save the sediment for later consultation of a more experienced ‘uroscopist’.

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R. A. P. Koene


A case of early-onset pre-eclampsia associated with IgA nephropathy

Sir,

A 31-year-old healthy Japanese woman presented to an obstetrician in September 1996 with amenorrhoea and was found to be pregnant (7th week of gestation). In November 1996 (16th week of gestation), she weighed 56 kg, which represented a gain of 2 kg over her normal weight. Pretibial oedema was noted. During the 19th week of gestation, she weighed 70 kg and anasarca was noted. She consulted another obstetrician who noted a positive test for proteinuria and haematuria, hypoprothrombinaemia and hypoalbuminaemia, and hypertension. She was transferred to our hospital with a diagnosis of severe pre-eclampsia. On admission, the serum creatinine (s-Cr) was 141 μmol/l (normal range in pregnant women: 35–71 μmol/l), blood urea nitrogen (BUN) 5.3 mmol/l, uric acid 9.55 mg/dl (normal: 3.0–6.0), total protein (TP) 44 g/l and albumin 18 g/l in blood chemistry. Her urine gave a +++ test for proteinuria and haematuria (RBC 5–10/high-power field), but was negative for glycosuria. The 24-h urinary protein (UP) was 5.5 g. To determine the aetiology of the hypertension, a plasma renin and aldosterone, and thyroid function tests were all within normal limits.

She was treated with antihypertensive agents, but blood pressure was not controlled. During the 20th week of gestation, she decided to discontinue the pregnancy and the fetus was aborted. Her blood pressure returned within the normal range rapidly, and 2 weeks later she did not require any antihypertensive agents. Three weeks later, blood chemistry revealed that a TP of 54 g/l, albumin of 28 g/l, s-Cr of 76 μmol/l, and BUN of 2.5 mmol/l, and urinary tests revealed a UP of 0.7 g/day.

A renal biopsy was performed 3 weeks after the abortion. The specimen revealed segmental sclerosis, visceral epithelial caps, a double-contour appearance, swelling of the endothelium, adhesions, and mesangial deposits. In an immunofluorescence (IF) study, staining for antibodies against IgA, IgG, and C3 was positive in the mesangial area, while staining for IgM, C1q, C4, and fibrinogen was negative. Electron-microscopy revealed fusion of foot processes, swelling of endothelial cells, matrix widening, and mesangial dense deposits without mesangial proliferation (Figure 1). These results were consistent with IgA nephropathy and nephropathy of pre-eclampsia.

Pre-eclampsia is thought to produce renal alterations such as endothelial swelling and ballooning of the glomeruli, similar to focal glomerulosclerosis. In the present case the onset of proteinuria, generalized oedema, and hypertension occurred during the 18th week of gestation, and the hypertension and oedema disappeared 2 weeks after delivery. The pathological findings in renal biopsy are characteristic of the nephropathy of pre-eclampsia, while that mesangial deposits and IF findings are characteristic of IgA nephropathy. These results show that IgA nephropathy and nephropathy of pre-eclampsia coexisted in this patient. There is no evidence,
however, that patients with IgA nephropathy are at particular risk of developing pre-eclampsia.

We conclude that the present patient had underlying IgA nephropathy associated with pre-eclampsia. We recommend that renal biopsy be performed after severe and/or atypical pre-eclampsia to reassess the renal risk of further pre-eclampsia.

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Acute renal failure in patients with multiorgan failure: risk factors influencing survival

Sir,
The mortality of acute renal failure (ARF) still exceeds 50% (it can reach up to 80% in Intensive Care Unit patients), and so does the mortality of several forms of multiorgan failure (MOF) [1]. Mortality of ARF seems to be determined by the severity of associated diseases rather than by the ARF itself. Because of the high mortality rate and enormous treatment costs, from early days much interest has been shown in determining the prognosis of these patients. With this aim, multiple aspects have been studied [2]. There is a debate in the literature about the usefulness of different patient characteristics and score systems in predicting the outcome of ARF patients of Intensive Care Units (ICU) [3,4]. The aim of the present study was to evaluate character-istics and indices suited to predict mortality in MOF patients with ARF.

We studied retrospectively data of 39 patients with MOF requiring renal replacement therapy, admitted consecutively to the ICU of our Medical Centre from April 1, 1994 to December 31, 1996. This was a mixed population of medical and surgical patients. All were treated with intermittent haemodialysis carried out with cuprophane or polysulphone filters. We considered only death or discharge from ICU as valid outcomes. Student’s t-test and χ²-test were used to assess whether individual variables differed significantly between survivors and non-survivors at a P < 0.05.

The overall mortality rate was 74.3%. The mean age of the patients was 53 ± 18.8 years. There was no difference in age, gender, serum creatinine, urea nitrogen, serum potassium, and blood pressure between survivors and non-survivors at the time of the initial renal consultation. The APACHE II score at the time of the initial renal consultation was significantly higher in non-survivors than in survivors (28.8 ± 5.50 vs 21.0 ± 2.79, P < 0.005). The number of organ system failure (OSF) [5] was 2.4 ± 0.97 in survivors and 3.1 ± 0.90 in non-survivors (P < 0.05). Survivors had higher hematocrit (30.8 ± 5.29 vs 24.6 ± 4.87, P < 0.05), higher serum total protein (58.9 ± 9.04 g/l vs 48.0 ± 7.88 g/l, P < 0.005) and serum albumin levels (31.9 ± 2.52 g/l vs 27.4 ± 4.31 g/l, P < 0.015) than non-survivors. Scopsis occurred in 45% of the non-survivors and 30% of the survivors (P < 0.01). Sixty-two per cent of the non-survivors and 40% of the survivors (P < 0.01) were oliguric at the time of the initial renal consultation. Forty-nine per cent of the survivors and 76% of the non-survivors needed mechanical ventilation (P < 0.01). Thirty per cent of the survivors and 56.8% of the non-survivors received vasopressor drugs because of hypoten-sion when first seen by nephrologists.

In conclusion, the high mortality rate observed in our patients is comparable to those reported in the literature. Our series shows that MOF patients with lower hematocrit, serum albumin or serum total protein, having sepsis or being oliguric, needing vasopressor drugs or mechanical ventilation seem to have higher death rate. APACHE II score and the number of OSF at the time of the initial renal consultation appear to be useful in predicting the outcome in these patients. Survival seems to be negatively linked to the severity of associated diseases.

It would be desirable to start prospective multicentre studies with the purpose of determining patient characteristics and score systems applicable in predicting the outcome in MOF patients with ARF.

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University Medical School of Pécs
Hungary


Fucus vesiculosus: a nephrotoxic alga?

Sir,
In January 1995, a 18-year-old female was admitted to our unit because of polyuria and polydypsia. The patient complained of extreme faintness and her general condition was poor. The patient had been on a hypocaloric diet over the 3 months prior to the admittance and had actually lost ~10 kg in weight; as an adjunctive therapy prescribed by an herbalist, she was also taking marine oak (Fucus vesiculosus) in 400 mg tablets (three tablets three times a day). Her personal history was negative for renal diseases and she denied any other medication. Laboratory testing revealed: blood creatinine, 8.7 mg/dl; glycosuria (500 mg/dl); moderate proteinuria and leucocyturia; serum autoantibodies, negative. Renal sampling performed by automatic Trucut needle yielded moderate interstitial fibrosis, widespread tubular degeneration, and diffuse lymphohomonocytic infiltrate; the glomeruli displayed scarce and focal mesangial proliferation, but the basal membrane appeared as intact (Figure 1a). Direct IF testing was negative. Positive peroxydase staining was obtained for T-lymphocyte-related UCHL1 (CD45 RO) and monocyte-related KP1 (CD68) antibodies, respectively (Figure 1b, c).

To exclude contamination by heavy metals, we performed a quantitative analysis on the marine oak powder the tablets were composed of. For this purpose, we used an atomic adsorbance spectrophotometer (Varian Spectra-20) supplied with a graphite minipulse plus an autosampler; before testing,
cortical necrosis, but the most common pathologic feature is interstitial fibrosis, tubular atrophy, and lymphomonocytic infiltration [5,6]. In spite of a generally favourable prognosis, some cases of residual functional impairment have been described [7]. Our patient was completely cured 1 year after the disease onset, and at present time she is in good health.

In our country, the lack of an adequate regulation about the therapeutic sale of herbalistic products is probably based upon the false conviction that ‘natural’ products are harmless and that phytotherapy is henceforth to be preferred to ‘conventional’ medicine. In particular, the intake of marine alga preparations as an adjuvant principle in slimming diets has been progressively enhanced by the prescription-free sale. Although a direct nephrotoxicity of this drug might hardly be proven, its pathogenicity can be related to the content of heavy metals as an heritage of growth in heavy polluted water [8].

We hope that this report can stimulate the Italian Health Authorities to request similar licensing procedures for both synthetic drugs and ‘natural’ products.

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Feasibility of a native arteriovenous fistula as the initial type of permanent vascular access in the majority of chronic haemodialysis patients

Sir,

The April 1997 issue of NDT brought two contributions [1,2] concerning the impact of vascular access on morbidity and mortality of the chronic haemodialysis patients. Woods and Port stated in an Editorial Comment [1] that despite evidence showing the superiority of a native AV fistula over an AV graft because of lesser complication incidence and a longer life, a trend has been documented in the United States away from use of an AV fistula and towards use of an AV graft. As a result <30% of the American patients [3] have

samples were pre-digested with concentrated nitric acid. Chemical quantitative analysis gave the following results: arsenic, 21.3 mg/kg; cadmium, 0.3 ppm; mercury, 0.06 ppm; and chrome, 4 ppm.

The real incidence of ‘heavy metal nephropathy’ is not known because the clinical presentation is non-specific and renal biopsy is necessary to confirm the diagnosis [1–6]. Arsenic can evoke either an acute tubular necrosis or a

Fig. 1. (a) Renal biopsy specimen showing moderate interstitial fibrosis with widespread lymphomonocytic infiltrate (PAS 250×). (b) Renal biopsy specimen: immunohistochemistry with UCHL 1 (CD45RO) antibody showing interstitial T-lymphocytes (avidine-biotin-peroxidase 250×). (c) Renal biopsy specimen: Antibody KP 1 (CD68) revealing interstitial monocytes (avidine-biotin-peroxidase 250×).
an AV fistula. It is explained by an ageing haemodialysis population, increasing number of diabetics, and also by late patient referral [3,4]. In this context the Woods and Port mention that an AV graft can be used for haemodialysis soon after placement while an AV fistula may take 2–3 months to mature.

Based on our own experience we believe that the above opinions are too categorical. At present, our haemodialysis program at the Wroclaw University Hospital and in the cooperative units encompasses 256 patients: 111 females, 145 males, aged 10–75 years, mean ± SEM 48.3 ± 9.9 years.

Native AV fistula was attempted in all persons. We prefer end-to-end anastomosis between the cephalic vein and the radial artery which permits avoidance of an arterial ‘steal’ and venous ‘stasis’. This variant of AV fistula was accomplished in 228 patients. In the patients with destroyed superficial veins on the anterior aspect of the forearm the radial artery was anastomosed end-to-end with the perforating vein (five patients), with the basilic vein which was transposed under the skin (five patients), or an ulnaris fistula was made, connecting end-to-end the basilic vein to the ulnar artery (three patients). The first attempt was successful in 193 patients (75%). The procedure was repeated with success in 48 patients (19%). On the whole, the functioning AV fistula on the forearm was created in 241 patients (94%, 103 females, 92.8% success rate; 138 males, 95.2% success rate) in whom 315 operations were performed (1.3 operations per patient).

On average, 2 weeks elapsed from the shunt operation to the first dialysis, but in some patients the fistula was cannulated on the next day following formation.

The known risk factors for the failure in the creation of the native AV fistula include, besides female sex, age > 65 years and underlying diabetes mellitus. In our haemodialysis population there were 32 patients > 65 years of age (mean age 71 ± 1.1 years). In this group a native AV fistula was successfully created in 31 patients after 1.4 operations per person.

Our experience with diabetics is based on the results obtained in 37 patients with end-stage diabetic nephropathy (mean age 52.2 ± 2.3 years, type 1 in 28 patients, type 2 in nine patients). The successful native fistula development was achieved in 35 patients (an average of 1.4 operations per person).

Our data prove that a native AV fistula is continuously the technically feasible permanent vascular access in the majority of chronic haemodialysis patients. We are conscious that our haemodialysis population is younger than in the US and Western Europe. However, we share the opinion [5] that the so-called centre effect connected with operative skill and experience is also a very important part of the success. All the operations in our patients were performed by two nephrologists.

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5. Prischl FC, Kirchgatterer A, Brandstatter E et al. Parameters of

Relationship between haemoglobin, ristocetin-induced platelet aggregation and platelet surface glycoproteins GPIb and GPIIb/IIIa in haemodialysis patients under therapy with recombinant human erythropoietin

Sir,

We have read with great interest the paper from Borawski et al. in a recent issue of *NDT* [1]. The authors found a significant inverse correlation between ristocetin-induced platelet aggregation and haemoglobin (Hb) concentration in 28 haemodialysis (HD) patients treated with recombinant human erythropoietin (rHuEpo). They conclude that enhanced platelet aggregability to ristocetin could indicate blunted erythropoiesis in HD patients treated with rHuEpo: furthermore they hypothesize that ristocetin-induced platelet aggregation may reflect the presence of inflammation, which is often followed by development of anaemia due to increased generation of inflammatory cytokines with inhibitory activity on erythropoiesis. Platelet aggregation in response to ristoce- tin is a reliable measure of platelet–vessel wall interactions. Key points of such interactions are the platelet surface receptors GPIb (the receptor for von Willebrand factor, vWF) and GPIIb/IIIa (the receptor for fibrinogen). When the damaged subendothelial matrix, which contains a large amount of vWF multimers, is exposed to flowing blood, platelets initially adhere through the interaction between vWF and GPIIb/IIIa. A reduction of platelet glycoprotein GPIb expression in uraemia was reported by various authors and by our group [2,3]; this alteration plays an important role in the pathogenesis of uraemic bleeding (defect in primary haemostasis). In HD patients GPIb/IIIa glycoprotein expression is enhanced or similar to normal controls, but this integrin shows an inability to undergo a conformational change during platelet activation [4]. These acquired platelet receptorial defects are present since the early stages of renal failure and are not corrected by the haemodialysis procedure, while peritoneal dialysis seems to correct the defective expression of the GPIb/IIIa glycoprotein [5]. In a recent paper we reported that the expression of these platelet receptors may be related to the prothrombotic tendency of HD patients who suffer from more occlusive and thrombotic events of the arteriovenous fistula [6]. Therapy with rHuEpo produces an increase in the expression of the glycoprotein GPIb [7] and this effect could explain the abnormal procoagulant response to this drug in uraemic patients. According to Borawski findings, we wished to correlate the expression of glycoproteins GPIb and GPIIIa/IIa to the concentrations of Hb in 11 stable HD patients (five males, six females, age 29–68 years) treated with rHuEpo since almost 3 months and 14 HD patients (seven males, seven females, age 32–69 years) without rHuEpo therapy. Cuprophane-type dialysers were used and the groups did not significantly differ in antihypertensive therapy, heparin dose, lipid metabolism. No antiaggregant drug was used, no patient was suffering from diabetes. Early morning, 4.5 ml of venous blood was taken from each subject. Cytofluorometric investigations were performed on all samples to quantify the expression of the platelet surface receptors, the glycoproteins GPIIb and GPIIIa/IIa, using specific fluorescent monoclonal antibodies CD42 and CD41 (Immunotech, Marseille, France) and a FACscan cytofluorimeter (Becton-Dickinson, USA).
The blood was mixed with 0.5 ml citrate Na 0.129 M and centrifuged 10 min at 400 rpm at room temperature to obtain platelet rich plasma (PRP). The total PRP was centrifugated, the pellet was washed twice for 10 min at 700 g with Clay-Adams solution (CellWash) then diluted with the same solution in order to obtain a number of platelets equal to 50,000/mm³ in each part. To each of the samples 10 µl of monoclonal antibodies CD42 and CD41 was added. All the tubes were then stirred with a vortex mixer and incubated for 10 min at room temperature. The tubes were rinsed twice with CellWash solution, then centrifuged at 700 g, and the pellet was again suspended with 0.5 ml of the same solution. Finally readings on the cytofluorimeter were taken, after proper calibration by logarithmic amplification of the mean fluorescence and mean flow.

We found no correlation between the expression of platelet surface glycoproteins GPIb and GPIIb/IIIa and Hb (Figure 1). A positive correlation between the expression of GPIb, GPIIb/IIIa receptors and the required dose of rHuEPO to reach the target haematocrit was observed (Figure 2). Our data are partially conflicting with the Borawski report: the expression of the platelet surface glycoproteins GPIb and GPIIb/IIIa does not seem to play a role in determining the hypothesized mechanism of blunted erythropoiesis in HD patients on rHuEPO therapy.

Other elements involved in platelet aggregation in response to ristocetin could explain the hyporesponsiveness to rHuEPO in uraemic patients with ristocetin-induced platelet hyperaggregability: we have measured the antigenic expression of GPIb and GPIIb/IIIa, whereas Borawski et al. have
Fig. 2. Correlation between the expression of platelet glycoproteins GPIb and GPIIb/IIIa (expressed as mean flow ± SD) and the required dose of rHuEPO to reach the target haematocrit.

reported functional data. Furthermore we want to stress the important role of platelet surface receptors in the relationship between platelet reactivity, hypertension and rHu-EPO therapy in haemodialysis patients. The increased expression of platelet surface glycoproteins during rHu-EPO therapy has been confirmed by many authors [4,7,8] and the possible risk in producing artefacts has been reduced by the modern technology and by the accuracy of the operators. In conclusion the platelet receptorial defects of uraemic patients may play an important role in uraemic bleeding and accelerated atherosclerosis and can offer an acceptable explanation of many clinical problems in the field of renal failure.
8. Ozsoylu S, Gurses T. Von Willebrand factor and rise in ristocetin co-factor with erythropoietin. Lancet 1993; 341: 1221

Parapoxvirus orf in kidney transplantation

Sir,
A 44-year-old male Moslem of North-African origin presented in 1989 with an ANCA-negative rapidly progressive glomerulonephritis, complicated by convulsions and mononeuritis multiplex. An arteriography of the abdominal vessels showed numerous aneurysms and the kidney biopsy revealed crescents and fibrinoid necrosis, suggesting polyarteritis nodosa. Immunosuppression with corticosteroids for 2 years and cyclophosphamide for 8 months was installed. Arterial hypertension was treated with felodipine (10 mg/d) and ramipril (2.5 mg/d). Despite treatment, 3 years later the patient developed end-stage renal failure and haemodialysis was started. By that time he was already hepatitis C positive. Fourteen months later he was transplanted with a cadaveric kidney and early transplant function was satisfying under a therapy with corticosteroids (25 mg/d prednisolone), azathioprine (2 mg/kg/d) and cyclosporin (5 mg/kg/d). Two months after transplantation he developed purpura, arthralgia, fever and renal failure (serum creatinine: 2.5 mg/dl) with proteinuria of <2 g/day. Circulating immune complexes and polyclonal cryoglobulins appeared. The kidney biopsy demonstrated mesangial hypercellularity and thickening of the capillary walls. The diagnosis was compatible with a membranoproliferative glomerulonephritis caused by hepatitis C-associated cryoglobulins. Renal function slowly deteriorated and in March 1995 the patient had a serum creatinine of 2.5 mg/dl, a creatinine clearance of 35 ml/min and proteinuria of 3 g/day.

It was at this time that we first recognized a hypertrophic lesion with central necrosis at the right thumb. The patient recalled having cut himself in the thumb, while sacrificing a lamb at the Moslem ritual sacrifice. This lesion was microscopically confirmed as being Orf infection: epidermal multilayered keratinocytes with central necrosis and multinucleated giant cells. Usually in this setting—of MHC class II dermal dendritic cells was inhibited. IL-2 and interferon-γ mRNA were suppressed, which is consistent with the immuno-suppressive effect of cyclosporin. TNF-α was not inhibited. So, adequate cellular immunity is mandatory for clearing orf virus.

We presented here the case of a kidney transplant recipient under therapy with cyclosporin, in whom immunity against this particular virus was abrogated, just like in the experimental condition. The patient had multiple relapses of this infection before cure. It is also the first description of orf virus infection in a transplanted patient.

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Long-term bone densitometry post-replacement transplantation in patients treated with either cyclosporin or prednisolone

Sir.
Bone loss is recognized in the immediate post-operative period following renal transplantation [1,2]. Prednisolone is thought to be an important factor in this process. Changes of bone densitometry in the longer term are less well recognized and the role of cyclosporin in this process is difficult to establish as most current immunosuppressive regimens combine cyclosporin and prednisolone. This renal unit was involved in the early clinical trials of cyclosporin. The protocol required treatment with either cyclosporin or prednisolone and azathioprine and there remains a group of patients with renal function stable for many years who have not been treated by cyclosporin and prednisolone in combination.

We have performed a cross-sectional uncontrolled observational study of lumbar, femoral neck, and total body bone mineral densities (BMD) in 42 renal graft recipients who had been transplanted over 5 years previously (median 13,
Rhabdomyolysis and acute renal failure associated with Salmonella enteritidis bacteremia

Sir,

Rhabdomyolysis is a clinical syndrome characterized by serum elevation of creatine phosphokinase (CPK) and myoglobinuria leading to acute renal failure. This entity can be precipitated by different causes [1]; a certain proportion of cases have an infectious etiology [2,3]. Rhabdomyolysis is a rare complication of salmonellosis. Only six cases were reported in a recently published review [3].

A 56-year-old man presented with a 2-day history of oligoanuria and severe metabolic acidosis. One week before admission he had had high fever (39–40°C), anorexia, chills, headache and confusion. There was incidence of muscle overexertion. He had mild hypertension treated by 5 mg Amlodipine BID and an unremarkable family history.

Examination revealed a distressed man with diffuse haemorrhagic exanthema and kussmaul breathing; his temperature was 38.5°C, pulse rate was 115 b.p.m. and BP was 100/70 mm Hg. Muscles were painful on palpation, especially proximal muscles of upper and lower extremities and there was reduced muscle strength. Initial laboratory study disclosed the following data: haematocrit 44%; WBC 16 900/μl (90% neutrophils); platelets 125 000/μl; urea 508 mg/dl; creatinine 19.32 mg/dl; uric acid 17.3 mg/dl; serum sodium 139 mEq/l; potassium 6.2 mEq/l, calcium 8.15 mg/dl; inorganic phosphate 5.6 mg/dl; total protein 6.2 g/dl (albumin 3.0 g/dl); CPK 8800 IU/l; LDH 1400 IU/l; aspartate aminotransferase 195 U/l and alanine aminotransferase 42 U/l. Arterial blood gas determination revealed a pH of 7.14 and a base excess of −18 mEq/l. Urine was red-brown in colour, protein was +2 by dipstick and the qualitative test for myoglobin gave a strong positive reaction.

The patient was treated with haemodialysis for 6 days whereby the patient improved, CPK levels decreased, urine output increased and urine became clear. Blood cultures received at the first day of hospitalization yielded Salmonella enteritidis and therapy with Ciprofloxacine 200 mg b.i.d. was started. Widal agglutination reaction was positive in high titters (1:3200) on the 12th day of the disease. Two weeks later the patient recovered completely and he was discharged from the hospital with normal renal function (serum creatinine level 0.98 mg/dl).

The spectrum of infectious agents that have been reported to cause rhabdomyolysis is broad including viruses, bacteria, parasites and fungi [3]. Salmonellosis associated with rhabdomyolysis has been reported only in six cases in the literature. Acute renal failure occurred in four out of six (67%) patients reported. Salmonella sp. is suggested to cause muscle damage by direct bacterial invasion as well as by decreasing the oxidative and glycolytic enzyme activity of skeletal muscles and by activating lysosomal enzymes [4].

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