evidence of diabetic retinopathy, neuropathy, or nephropathy (Albustix —) in any of the patients. Eight healthy men matched for age (mean 25 ± 1 years) and body size (weight 76 ± 3 kg, height 182 ± 2 cm) served as controls.

All patients were admitted to Helsinki University Hospital and during the first four days received their usual dose of insulin. On the third day diurnal blood glucose values were determined and urine collected for measurement of glucose, albumin, and β_2 -microglobulin excretion.² In the urinary albumin measurement the sensitivity of the method was $25 \mu\text{g/l}$ and the coefficients of interassay and intra-assay variation were 6.8% and 3.1% respectively. On the fourth day the patients performed a 40-min cycle ergometer exercise test, starting at 9 am.

On the fifth day a constant subcutaneous insulin infusion was started with a portable, battery-driven infusion pump (Model AS2C, Auto-Syringe Inc, Hooksett, New Hampshire, USA). We used an initial basal infusion rate of 0.2 mU insulin/kg/min. The remainder we gave as bolus injections before meals to provide 30–35% before breakfast, 25% before lunch, 30–35% before dinner, and 5–10% before evening snack, as described.⁴ After initial stabilisation on the regimen for four days the infusion was continued for 14 days, during which the patients remained in hospital. The postinfusion studies were carried out on the last two days of infusion.

Mean diurnal blood glucose concentrations, measured at two-hour to four-hour intervals, fell after two weeks of insulin infusion from 9.3 ± 0.7 mmol/l (168.0 ± 12.6 mg/100 ml) to 5.7 ± 0.4 mmol/l (103.0 ± 7.2 mg/100 ml) ($p < 0.005$); the control value, however, was 4.1 ± 0.1 mmol/l (74.0 ± 1.8 mg/100 ml); ($p < 0.005$). Urinary glucose excretion fell from 233 ± 67 mmol/24 h (42 ± 12 g/24 h) to 11 ± 5.5 mmol/24 h (2 ± 1 g/24 h) after two weeks of infusion treatment ($p < 0.01$). With the improvement in metabolic control insulin requirements declined by 28% ($p < 0.02$).

Albuminuria in the resting state fell by 39% from $5.2 \pm 0.4 \mu\text{g/min}$ to $3.5 \pm 0.6 \mu\text{g/min}$ ($p < 0.05$) after two weeks of pump infusion treatment (figure). Nevertheless, there was definite overlap between diabetic and

restored to normal. The decrease in albuminuria was associated with near-normal diurnal blood glucose concentrations and virtual elimination of glucosuria.

Enhanced albumin excretion may be due either to augmented glomerular filtration or to decreased tubular absorption of albumin, or to both. In this study no change in urinary β_2 -microglobulin excretion (which reflects tubular reabsorption) was observed after pump infusion treatment. These data thus suggest that the correction of exercise-induced albuminuria was achieved primarily by a reduction in the glomerular permeability to albumin.

Though albumin leakage has been thought to contribute to the thickening of glomerular basement membrane,⁵ the exercise-induced increase in albuminuria has no known structural implications. It will be interesting to see if long-term correction of albuminuria by strict metabolic control with continuous insulin infusion prevents or delays the onset of irreversible structural nephropathy in juvenile-onset diabetes.

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Urinary albumin excretion at rest and after exercise in healthy subjects and diabetic patients during conventional treatment and after two weeks of continuous subcutaneous insulin infusion. Chart shows individual values and means $\pm$ SEM. * $p < 0.05$ v resting value during conventional treatment. † $p < 0.02$ v exercise value after pump infusion or in control subjects.

control values, and neither preinfusion nor postinfusion levels in diabetic patients differed significantly from those in controls ($4.9 \pm 0.4 \mu\text{g/min}$). The exercise-induced rise in albuminuria in the diabetic group during conventional treatment ($3.0 \pm 0.7 \mu\text{g/min}$) was 3.8-fold greater than in the healthy controls ($0.8 \pm 0.7 \mu\text{g/min}$) ($p < 0.05$). Thus the mean postexercise value in diabetics ($8.1 \pm 0.8 \mu\text{g/min}$) was 42% higher than in controls ($5.7 \pm 0.6 \mu\text{g/min}$; $p < 0.02$). After two weeks of pump infusion treatment the exercise-induced rise in albuminuria in diabetic subjects ($0.8 \pm 0.5 \mu\text{g/min}$) was indistinguishable from that in controls, and the postexercise values were comparable in the two groups. Urinary β_2 -microglobulin secretion in diabetic patients remained unchanged during pump infusion treatment, both at rest (60 ± 9 ng/min before v 73 ± 12 ng/min after treatment) and during exercise (77 ± 9 ng/min v 87 ± 13 ng/min). The relative exercise intensity employed was similar in patients and controls, as reflected by a comparable rise in heart rate (to 136 ± 3 v 138 ± 1 beats/min) and blood lactate concentrations (to 3.2 ± 0.6 mmol/l (29.0 ± 5.4 mg/100 ml) v 2.6 ± 0.4 mmol/l (23.4 ± 3.6 mg/100 ml)) respectively in diabetic and control subjects.

Comment

Before starting pump infusion treatment the patients had albumin excretion in the high-normal range at rest, whereas in response to exercise it was significantly raised. After two weeks of insulin infusion treatment, however, the exercise-induced rise in albuminuria was

Intravascular haemolysis with acute renal failure after angiocardiology

Complications of coronary angiography are uncommon and usually cardiovascular.¹ We report a case of intravascular haemolysis with acute renal failure after angiocardiology.

Case report

A 58-year-old blacksmith presented with a three-year history of retrosternal pain on exertion. Electrocardiograms were normal at rest and on exercise. He had mild hypertension controlled with methyldopa and a thiazide diuretic but no history of renal disease and was not diabetic. His pain, which initially responded to conventional medical treatment, progressed to limit his exercise tolerance to 30 yards (27 m). On admission his haemoglobin concentration, white cell and platelet counts, reticulocyte index, urea and electrolyte values, serum creatinine concentration, and chest x-ray picture were within normal limits. Routine urine analysis showed no abnormality.

Left ventricular angiography was performed with 50 ml (0.75 ml/kg) Urografin 370 (an aqueous solution of sodium diatrizoate 66% w/v and meglumine diatrizoate 10%) injected at 12 ml/s. Selective coronary angiography was then carried out using a further 80 ml of the same contrast medium. The patient was nauseated for 12 hours after the procedure but slept normally that night. Next morning he was clinically jaundiced, though there were no new findings on physical examination. He voided 10 ml of black urine and became severely oliguric. No erythrocytes were seen on urine microscopy but the sample contained protein ++, blood +++, urobilinogen +++, and bilirubin + on stick testing. The blood urea concentration had risen from 4 mmol/l (24 mg/100 ml) to 23.8 mmol/l (143 mg/100 ml), and the plasma concentration of unconjugated bilirubin had risen from 14 mmol/l (0.81 mg/100 ml) to 138 mmol/l (8 mg/100 ml). There was no appreciable change

in liver transaminase or alkaline phosphatase activity. Haemoglobin concentration fell from 14.2 g/dl to 12.8 g/dl with a rise in reticulocytes to 3%. Intravascular haemolysis was confirmed by a positive methaemalbumin test, a raised plasma haemoglobin concentration at 0.26 g/l (normal range 0.01-0.04 g/l), and a reduced haptoglobin concentration at 0.028 g/l (normal range 0.3-2.0 g/l). The platelet count had fallen to $33 \times 10^9/l$, but a clotting screen was normal. Coombs test was negative.

A diagnosis of acute intravascular haemolysis with associated renal failure was made. Despite alkalinisation of his urine he remained anuric and the blood urea concentration rose to 48.3 mmol/l (290 mg/100 ml). He was transferred to the renal unit, where he required haemodialysis on six occasions over the next 10 days before entering a diuretic phase. Values of plasma haemoglobin, haptoglobins, reticulocytes, platelets, bilirubin, and urea returned to normal and remained so after termination of dialysis. Three months after discharge serum haptoglobin values, Schumm's test, Ham's test, haemoglobin electrophoresis, Coombs test, and red-cell enzyme activities were normal. There was evidence, however, of an increase in osmotic fragility (lysis beginning at 0.75% NaCl solution, control 0.55%).

Comment

Acute renal failure is a well-recognised complication of radio-contrast investigations but the mechanism is usually unknown.² Diabetes mellitus and pre-existing renal insufficiency appear to be predisposing factors but these were not present in our patient.

Haemolysis and haemoglobinuria after contrast angiography has been documented in six children with cyanotic congenital heart disease and secondary polycythaemia.^{3,4} Martin⁵ reported a case of acute renal failure with low serum haptoglobin values and methaemoglobinuria after myelography with sodium diatrizoate. It has been postulated³ that rapid injection of hypertonic contrast medium causes initial loss of water and uptake of solute in the red blood cells. When isotonicity of the plasma is restored these erythrocytes may absorb excess water, swell, and be more easily haemolysed. That our patient had abnormal osmotic fragility three months after discharge suggests that he may have been susceptible to sudden increases in plasma tonicity. Intravascular haemolysis is thus a potentially serious, though fortunately rare, complication of contrast media investigations.

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Possible transmission of malaria by renal transplantation

Malaria may present as a postoperative fever. This may be due either to infection by transfusion¹ or, in patients from endemic areas, to recrudescence of latent infection provoked by the surgery.² I report a case of malaria in a recipient of a renal transplant in which the infection may have been acquired from the donor kidney.

Case report

A 27-year-old Saudi man was admitted to this hospital on 17 December 1979 for living-donor renal transplantation. He had chronic renal failure of uncertain aetiology and had been on regular haemodialysis in Saudi Arabia for one year. Examination showed no other abnormality apart from a late systolic murmur. His brother, the donor, was 25 years old and in good health. Neither gave a definite history of malaria but both came from Jizan, a known

malarial area of Saudi Arabia, and the donor was resident there. The donor was found to have mild splenomegaly for which no cause was found despite extensive investigations, including examination of blood films for malaria parasites.

On 29 December 1979 renal transplantation was performed and standard treatment with prednisolone and azathioprine begun. Good renal function was established immediately, with serum creatinine concentration falling to normal within three days. The postoperative course was uneventful apart from a dehiscence of the abdominal wound. Low-grade fever was noted, but no cause was found and the patient was discharged well on 21 January 1980.

On 6 February he was readmitted with aching in limbs and chest, occasional rigors, and a daily fever up to 38.5°C. Serum creatinine and urea concentrations rose and he was thought to be having an episode of rejection. Accordingly intravenous methylprednisolone was given, with subsequent return to normal of creatinine and urea values but without effect on his fever. On 22 February very occasional malaria parasites (*Plasmodium falciparum*) were seen in the blood film. Chloroquine was given and resulted in complete resolution of his illness.

Retrospective examination of a blood film from the donor taken the day before transplantation disclosed very scanty ring forms of *P falciparum*. No parasites were seen in the recipient's blood film on three occasions before the operation, though thick films were not available. The malaria indirect fluorescent antibody test was performed on available sera, and the table gives the results. This test is the most specific method of detecting malaria antibodies. Two antigens were used—*P falciparum* and *P fieldi*, which is a simian plasmodium found to be antigenically closely related to *P vivax*, though there is cross-reactivity between all human and some simian plasmodia.³ High titres ($\geq 1/200$) suggest recent infection in non-immune patients but may be associated with latent subclinical infection in those from hyper-endemic areas.

Results of indirect fluorescent antibody test on sera from transplant recipient and donor

	Date	Titre to <i>P falciparum</i>	Titre to <i>P fieldi</i>
Recipient	14 June 1979	4096	256
	17 December 1979	4096	1024
	25 February 1980	4096	1024
Donor	29 December 1980	16304	4096

Comment

One previous case of malaria occurring in a renal transplant recipient has been reported,⁴ though several cases have been described after cardiac surgery,⁵ which were possibly due to recrudescence of a latent infection provoked by the stress of the operation. In this case the infection might also have been due to recrudescence provoked by surgery, and the high initial indirect fluorescent antibody test titres in both patients suggest that latent subclinical infection was present in both. The infection may, however, have been acquired from the donor in view of his very high titres before the operation, and, though a new infection usually causes a rise in titre against the homologous antigen, and possibly against the heterologous antigen also, this may have been prevented by immunosuppression.

Whatever the source of infection, the important conclusion is that malaria must be added to the long list of causes of fever in renal transplant recipients and donors from malarial areas. Moreover, malaria is endemic in most of the coastal regions of Saudi Arabia, a country usually thought of as a non-malarial desert area. Both *P vivax* and *P falciparum* are found, but infections due to *P vivax* occur much more commonly.

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