deteriorating renal function were 211, 318, 329, 332 and 404 ng/ml. In addition, in another four cases (three patients)
a renal biopsy was performed because of worsening renal
function which showed evidence of cyclosporin A exposure
cytoplasmic vacuolation in tubular cells) and in one instance,
nephrotoxicity with vascular hyalisation. Trough concentra-
tions at biopsy were 170, 258, 272 and 273 ng/ml. On three of these occasions, Neoral dose reduction led to impro-
ving renal function and in the other case, where vascular
abnormalities were observed, dose reduction in combination
with intravenous methylprednisolone (for moderate cellular
rejection) was successful. In the 45 patients who received ren
allografts prior to our change to Neoral and followed
for the first 4 weeks, there were no cases of deteriorating renal
function which responded to Sandimmun dose reduc-
tion, and changes attributable to cyclosporin A exposure or
nephrotoxicity were observed in only one case on renal
biopsy, with a blood cyclosporin level of 545 ng/ml.
Achievement of a therapeutic plasma cyclosporin A in the
immediate post-transplant period is essential to reduce the
risk of acute rejection. Our clinical experience with Neoral
is that nephrotoxicity can occur with lower trough plasma
concentrations than we have observed previously with Sandimmun. Thus, our immunosuppression policy has now
changed so that all patients are commenced on Neoral 3
mg/kg in two divided doses and the dose adjusted to
maintain trough concentrations of 200–300 ng/ml. We feel
that our clinical observations are of relevance to physicians
managing renal allograft recipients and patients with glom-
erulonephritis receiving cyclosporin A.

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OKT3 monoclonal antibody therapy and visual loss

Sir,
In their report on visual loss complicating acute renal allograft rejection in a 30-year-old female Dr Jin et al. (Nephrol
Dial Transplant 1995; 10; 2144–2146) suggest this severe side effect to be related to OKT3 monoclonal antibody therapy.
Although some reports on ophthalmological problems following OKT3 administration have been published recently,
we believe that the presented data do not allow this conclusion [1,2].
The authors fail to exclude acute cytomegalovirus (CMV) infection which is well known to cause chorioretinitis with
perivascular infiltrates, exudates, and haemorrhage, and a permanent reduction in visual acuity [3,4]. The classical
lesions are due to vasculitis and often involve both macula and papilla. We base our argument on personal experience
with a renal transplant recipient who developed severe neuritis of both optic nerves, necrotizing retinitis and permanent
visual loss during an episode of otherwise subclinical CMV infection. This happened 10 days post-operatively when the
patient was on high-dose steroids and cyclosporin, but had not received OKT3.

The ophthalmological findings reported by Dr Jin et al. are compatible with those resulting from CMV infection
which is most common with potent immunosuppression. In their patient, accelerated rejection on the second post-
 operative day was unsuccessfully treated by a 6-day course of pulse methylprednisolone, before OKT3 was started on
the 8th post-operative day. CMV infection, for example, by transmission from the donated organ, may well have occurred
after more than a week of high-dose steroid therapy. It is not mentioned whether the donor was tested for anti-CMV
antibodies. Regrettably, the onset of visual disturbances was not noticed by the transplant physicians and the exact time
course is thus not known. Their patient retrospectively reported a 10-day period of slowly progressing ophthalmo-
logical problems 12 days after start of antibody therapy (7 days after stopping OKT3). At no time was acute CMV
infection ruled out as the underlying cause of the ophthalmological problems by investigation of direct CMV-antigen in
peripheral blood leukocytes, viral DNA by polymerase chain reaction, or CMV-specific IgM [5].
We conclude that the occurrence of ophthalmological problems in this particular patient cannot be clearly related
to OKT3 monoclonal antibody therapy. The underlying cause of visual loss could as well have been an ophthalmolo-
ic manifestation of acute CMV infection.

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Reply by authors

Sir,
CMV infection usually develops 4–6 months after trans-
plantation, probably reactivation due to prolonged immuno-
suppress. The patient preoperatively was IgG anti-CMV
antibody positive as usual transplant recipients in our centre.
We have not seen chorioretinitis in over 1000 patients includ-
ing over 200 treated with pulse solumedrol therapy.
Recently we studied CMV reactivation, and the results
were presented at the 4th Congress of Asian Society of
Transplantation (Dr Wie et al., August 1995). Using an
immunohistochemical assay for CMV antigenaemia in per-
ipheral blood, we found positive results in about 60% of
transplant recipients, but no chorioretinitis was detected in
high titre patients who also recieved solumedrol pulse therapy or
OKT3 therapy.

We did not study CMV in the reported retinitis case because
there were no other symptoms of CMV infection, e.g. fever,
leukopenia, CMV viral pneumonia, at the time
of retinitis detection, and the immuno-suppression was tapering and graft nephrectomy was planned.

In conclusion, we suggest the retinitis may be due to severe antigen-antibody complex vasculitis, which showed in the graft biopsy, but CMV reactivation after strong immuno-suppression such as OKT3 monoclonal antibody therapy cannot be excluded.

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The role of surgery and itraconazole in Aspergillus peritonitis in CAPD

Sir,
In their Case Report and review of literature, Tanis et al. [1] found only 13 cases of peritonitis which may be attributed to Aspergillus. In only five of these were there more than one positive culture and in only one were the classical hyphae seen. They also recommend catheter removal and antifungal agents. Nearly all patients had amphotericin B and only one had itraconazole as well. Recently we had an experience to suggest that catheter removal and amphotericin may result in inadequate treatment in a case of microscopy- and culture-confirmed Aspergillus peritonitis, and that surgical intervention in combination with prolonged use of itraconazole may be required.

The patient, a 37-year-old male presented with fever and generalized abdominal tenderness in June 1995. Before this visit, he had had a cough which was treated with antibiotics. He first presented in end-stage renal failure of unknown cause and was commenced on CAPD in January 1994. He was apyrexial with diffusely tender abdomen with rebound tenderness. Exit site and tunnel were normal. PD fluid was turbid with 920 w.b.c./µl (90% neutrophils). Gram-positive cocci were seen and the patient was treated with cephazolin and gentamicin i.p., which was changed on day 7 to vancomycin and amikacin i.p. because of lack of improvement. Previous dialysate cultures were negative. On day 13, the CAPD catheter was removed because of persisting symptoms and cloudy dialysate. Postoperatively the patient developed septicemic shock, requiring the addition of dopamine, cefotaxime and clexacillin intravenously. On day 18, PD fluid culture sent on day 13 showed Aspergillus niger, although the catheter tip sent for routine culture was negative. As the patient was well, no treatment was given.

By day 22, the patient was noted to have increasing ascites. Aspiration revealed a cloudy fluid with 2000 polymorphs/µl; staining revealed typical Aspergillus hyphae, which was confirmed on three subsequent samples. Amphotericin B (30 mg/day) was given intravenously. A repeat aspiration of the abdomen on day 50, revealed a persistently cloudy fluid with neutrophils, although fungal stains and cultures were negative. Abdominal ultrasound revealed multiple loculated collections. A surgical referral for open drainage was made. At laparotomy, the bowel was seen to be coated with fibrous capsule, and a large collection containing fibrin and turbid fluid was drained.

By day 65, after completing a cumulative dose of 1.5 g of amphotericin, the patient was well. As a small collection was seen on ultrasound, he was started on itraconazole 300 mg twice daily and discharged. The collection persisted and was noted to have increased in size to 10 x 10 cm. On day 120, straw-coloured fluid was aspirated, revealing 80 lymphocytes/µl, protein 51 g/l on examination, and was negative on culture. The patient was well on haemodialysis with no abdominal symptoms and an ESR of 38 mm/h. Itraconazole dose was reduced to 200 mg twice daily and a follow-up ultrasound arranged for 1 month.

It is reasonable to assume that the diagnosis is correct as hyphae were seen in several samples and Aspergillus confirmed on culture. Repeated bacterial and mycobacterial cultures were negative. The patient was not immuno-suppressed and the only risk factor appeared to be antibiotic usage. It is not certain whether Aspergillus is the primary cause of peritonitis or whether this developed after weeks on antibiotics. The source of the infection was also not clear, though this was not investigated thoroughly. After catheter removal, despite treatment with adequate dose and duration of amphotericin, the patient still required open drainage. The infection appears to induce a strong fibrous reaction, leading to formation of loculated collection which resulted in both poor drug accessibility and failure to return to CAPD. In retrospect, it cannot be certain whether surgery could have been avoided by earlier catheter removal and initiation of antifungal therapy.

As smaller collections persisted, long-term antifungal therapy was necessary. The role of itraconazole in treatment of fungal peritonitis is at present unclear. Certainly it is an effective oral agent against systemic aspergillosis [2] and has relatively few side-effects [3]. It is, however, poorly soluble in water and is not detected in the peritoneal fluid following oral administration [4]. On the other hand it is effective in cryptococcal meninitis despite low measurable concentration in the CSF, an effect explained by high meningeal concentration of the drug [3]. Although high levels of itraconazole have been measured in the omentum [5], there is scant data at present to support its use in fungal peritonitis. In this patient, after 60 days of treatment, he was well and fluid aspirated was clear, suggesting a possible role for itraconazole in the treatment of aspergillus peritonitis. Further studies may be useful to define its role in peritonitis due to fluconazole-resistant Candida species and Aspergillus.

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Influence of methodological differences on microbiological diagnosis of CAPD peritonitis

Sir,
Peritonitis is still the most important complication of continuous ambulatory peritoneal dialysis (CAPD) [1]. Different