taking cyclosporin (83 $\mu\text{mol/l}$ (range 69-103)) ($p=0.023$).

An intraindividual comparison was made and the median increase in T_{20} from the initial examination to the final examination (with an average of the left and right kidney changes) was 61% (range -41% to 267%) in the group treated with cyclosporin. In comparison, the T_{20} of the patients who were given a placebo fell by 12% (range -75% to 43%) ($p=0.0062$). The decrease in ^{51}Cr -EDTA clearance was larger (median fall of 23%, range -39% to 6%) in patients in whom the T_{20} had increased above the median increase in T_{20} (61%) than in the remaining patients treated with cyclosporin (fall of 1%, range -6% to 48%) and all the patients receiving a placebo (1%, range -10% to 27%) ($p=0.015$).

Comments

Because the renal clearance of hippuran occurs predominantly by tubular uptake and secretion, the increased T_{20} most probably resulted from a tubulopathy. Recent studies have suggested, however, that cyclosporin is not directly toxic to the tubular cells but that the tubulopathy is secondary to primary changes in renal haemodynamics.¹ We found no difference in the final ^{51}Cr -EDTA clearance, and, though the exact p value suggested a type II error, no significant change was seen when the patients treated with cyclosporin served as their own controls. Furthermore, no changes in the time taken to achieve maximal activity on the renograms were found. We therefore concluded that in the short term low dose cyclosporin does not interfere appreciably with renal haemodynamics. Nevertheless, the finding of increased values of T_{20} in the patients treated with cyclosporin suggests that the

tubular cells might be sensitive to small, and thus by the methods used here not readily detectable, changes in renal blood flow. This is in keeping with a slight, but significant, increase in the median plasma creatinine concentration of the group treated with cyclosporin (table), as creatinine is cleared by glomerular filtration and by tubular secretion.

Although these preliminary results might prove to have no biological importance—as opposed to statistical significance—we suggest that hippuran renography is an additional way of monitoring renal function in patients without transplants who are treated with cyclosporin.

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Split skin grafting in children with immune deficiencies

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A belief that healing will be poor in children with immunodeficiency disease may delay referral for surgical treatment of skin defects. We report on three children with an immunodeficiency or haematological disease complicated by chronic skin lesions in whom rapid healing was achieved by radical debridement and split skin grafting.

Case reports

Case 1—A 15 year old boy with a B cell leukaemia developed chronic graft versus host disease after receiving a bone marrow transplant. A large circumferential ulcer affecting most of his left lower leg resulted. Conservative treatment for six months was unsuccessful, and so surgical debridement and split skin grafting were undertaken; 75% of the graft took. The unhealed areas required further grafting, but complete healing was achieved in five weeks.

Case 2—A 4 year old boy with hyperimmunoglobulin E syndrome was referred with a three month history of a chronic soft tissue infection of the right thumb. An abscess at the site had been drained and debrided on several occasions. Conservative management with parenteral antibiotics did not produce any improvement. The thumb was then radically debrided and a split skin graft applied. Parenteral antibiotics were continued. The whole of the graft took, with complete resolution of the infection at one week.

Case 3—A 3 year old boy with a six week history of idiopathic acquired aplastic anaemia developed a necrotic ulcer over the right ulnar styloid. After one month of conservative treatment the lesion was excised and the defect covered with a split skin graft. Blood, platelets, granulocytes, and parenteral antibiotics were given perioperatively. The initial graft did not take, but further debridement and skin grafting resulted in complete healing at one week.

Comment

Two major phases are important in the success of skin grafting—namely, serum imbibition and vascularisation. The graft survives initially by absorbing serum from the host site, but within 48 hours endothelium grows into it and a circulation is established.¹ Any vascular bed may support a skin graft, but connective tissue denuded of its vascular covering will not (for example, tendon without paratenon).

In graft versus host disease immunocompetent T lymphocytes are introduced into an immunosuppressed, histoincompatible host. They recognise foreign host antigens, become activated, and attack host cells.² This occurs particularly in the skin. A healed skin graft will be susceptible to the same attack, but the initial take of the graft should not be compromised as T lymphocytes play no part in either serum imbibition or vascularisation. The hyperimmunoglobulin E syndrome is a primary immunodeficiency disease characterised by recurrent staphylococcal abscesses and an increased serum IgE concentration.³ This abnormal response to an antigen plays no part in the take of a skin graft and will not directly interfere with healing. Idiopathic acquired

aplastic anaemia is characterised by anaemia, leucopenia, and thrombocytopenia. The defect is cellular with an increased tendency to infection and bleeding.⁴ Although prejudicial to the success of skin grafting, it is not a contraindication provided deficiencies are corrected perioperatively, haemostasis is achieved before grafting, and the formation of haematoma is avoided afterwards.

Each of these children had a chronic cutaneous manifestation of a haematological or immunodeficiency disease. Healing was assumed to be abnormal because of a defect in either humoral or cellular defence mechanisms. This assumption delayed referral for

surgery by some months in each case, but debridement followed by split skin grafting produced rapid healing.

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Pneumonia associated with contact with cyanobacteria

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We report an outbreak of possible cyanobacterial poisoning after contact with water containing toxic *Microcystis aeruginosa* at a freshwater reservoir in Staffordshire, England, and give details of two cases of pneumonia that occurred after the water was swallowed.

Case reports

Case 1—A 16 year old army recruit was admitted on 26 September 1989 with a five day history of malaise, sore throat, blistering around the mouth, pleuritic pain on the left side, and a dry cough. He had also developed vomiting with central abdominal pain, followed by diarrhoea for one day. On examination he had a fever, with a temperature of 38.4°C. Examination disclosed signs of left basal consolidation, which was confirmed on chest radiography. He was tender in the umbilical area. The table shows the results of the laboratory investigations. He was treated with erythromycin and cefuroxime (owing to his sensitivity to penicillin), and his temperature settled within 24 hours. He remained periodically confused for two days with episodes of hallucinations but was well enough for discharge after one week.

Case 2—A 16 year old army recruit was admitted on the same date with a four day history of malaise, vomiting, sore throat, blistering around the mouth, dry cough, and pleuritic pain on the left side. He had

also developed central abdominal pain. On examination he had a fever, with a temperature of 39.2°C. Respiratory examination disclosed signs of left basal consolidation, which was confirmed by chest radiography, and abdominal examination showed epigastric and umbilical tenderness and tenderness in the right iliac fossa, with rebound tenderness. He was treated with penicillin and erythromycin, and his temperature settled within 24 hours. The tenderness in his right iliac fossa persisted for three days; the presumptive diagnosis was mesenteric adenitis. He was discharged after one week.

In both patients acute and convalescent serum samples showed no significant rise in antibody titre to leptospira, *Legionella pneumophila*, influenza virus A and B, chlamydia group antigen, *Coxiella burnetii*, *Mycoplasma pneumoniae*, and adenovirus. Repeat chest x ray films showed considerable resolution of the consolidation after one week.

Comment

The two recruits had taken part in canoe exercises lasting several hours in Rudyard reservoir, during which they swallowed some of the water. The water contained a mass development of cyanobacteria, dominated by *Microcystis aeruginosa*. Microcystin peptides^{1,2} were present in a sample of the bloom collected on 27 September 1989, and microcystin-LR was identified in the bloom material by high performance liquid chromatography.³ Reservoir water sampled on 9 October by the Public Health Laboratory Service contained counts of *Escherichia coli* considered to be unsuitable for bathing by European Community standards. There was no evidence of enterovirus contamination in water sampled on 2 October (National Rivers Authority, personal communication).

In the two cases described the patients presented with left basal pneumonia four to five days after taking part in a canoeing exercise. One (case 1) had difficulty sleeping that night and awoke the next morning with a sore throat, dry cough, vomiting, and abdominal pains, and the other developed similar symptoms within 24 hours and difficulty in walking.

In addition to liver damage in mice after microcystin intoxication, atypical pulmonary thrombosis has been observed, including pulmonary intravascular formation of protein deposits and removal of platelets from the circulation.^{4,5} The pulmonary consolidation and low platelet counts on admission (table) may have been a consequence of microcystin poisoning. (Platelet counts increased during treatment from $141 \times 10^9/l$ to $703 \times 10^9/l$ (case 1) and from $205 \times 10^9/l$ to $420 \times 10^9/l$ (case 2).)

Subsequently 16 soldiers were admitted to the medical centre at their barracks. Preliminary investigations showed that eight had been canoeing and had symptoms that might have been associated with cyanobacterial poisoning, including sore throats,

Results of laboratory investigations on patients with pneumonia after swallowing water from a freshwater reservoir

	Case 1	Case 2
White cell count ($\times 10^9/l$)	11.8	17.2
Total differential counts ($\times 10^9/l$):		
Neutrophils	10.30 (neutrophilia)	15.6 (neutrophilia)
Lymphocytes	0.52 (lymphopenia)	0.57 (lymphopenia)
Platelets ($\times 10^9/l$):		
26 September 1989	141	205
3 October 1989	703	420
Alanine transaminase (IU/l)	56	<35
Aspartate transaminase (IU/l)	94	<35
Blood gas tensions	Normal	Normal
Microbiological cultures:		
Blood	No growth	No growth
Sputum	Normal flora	Normal flora
Throat swab	Normal flora	Normal flora
Urine	No growth	No growth
Faeces	No enteric pathogens	No enteric pathogens
Leptospira enzyme immunoassay	Negative	Negative
Legionella indirect fluorescent antibody test (acute and convalescent serum samples)	<1.8	<1.8
Complement fixation tests for respiratory pathogens (acute and convalescent serum samples)	No significant rise in titre	No significant rise in titre