remains the gold standard for assessing suitability for transplant.

Procurement personnel must always consider the possibility of litigation whenever potentially diseased or defective organs are to be transplanted. Ordinary negligence liability may result if the disease or defect is discoverable with reasonable efforts using standard medical practices. Generally, the medical history is reviewed to rule out vascular disease, infection, or cancer, but further testing (e.g., biochemical, biopsy, autopsy, slit lamp exams of corneas, or coronary angiography in patients over 40) may be required as standard practice in some locales (21).

Vic
tims of cyanide poisoning have previously been described as suitable kidney (19) and corneal transplant donors, provided the corneoscleral tissue is rinsed thoroughly and maintained in a tissue-storage medium containing glucose (20). To our knowledge, however, this is the first report of successful multiple organ donation from a victim of cyanide poisoning. In this case, the lack of histological or biochemical evidence of irreversible cardiac, hepatic, or renal damage provided the basis for proceeding with multiple-organ transplantation over the objections of several surgeons.

In summary, we stress that careful donor evaluation and testing should be undertaken before excluding poisoned patients as suitable donor candidates. In the absence of transmissible disease and significant end-organ damage, mere presence or clinical effect of a toxicant should not automatically result in donor exclusion. Cyanide poisoning is only an example, and a rare one at that, of how the donor pool may be safely expanded. Brain death associated with exposure to carbon monoxide, hydrogen sulfide, azide, or oxidizing agents (causing methemoglobinemia) may also warrant evaluation for organ procurement. The nature and extent of testing required to exclude a poisoning victim will continue to evolve and will increasingly depend on what is known about mechanisms of cell injury initiated by a particular agent.

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PARVOVIRUS B19 INFECTION CAUSING PURE RED CELL APLASIA IN A RECIPIENT OF PEDIATRIC DONOR KIDNEYS1

Parvovirus B19, a recently discovered single-stranded DNA virus, is a known cause of chronic anemia in immunocompro-
myocarditis in a one-year-old child has been reported (1). Transient aplastic anemia has been reported in infected patients with congenital hemolytic anemia such as sickle cell disease (2), whereas chronic anemia affects immunocompromised hosts with acquired immunodeficiency syndrome (3) and acute lymphocytic leukemia (4, 5), and it has been reported in a 14-year-old girl following bone marrow transplantation (6). Only one previous report of parvovirus B19–producing anemia in a solid-organ transplant, that of a cadaveric renal transplant recipient receiving cyclosporine, appears in the literature (7).

We report the case of a pediatric en bloc renal transplant recipient on FK506 with pure red cell aplasia and peripheral pancytopenia caused by parvovirus B19 that were responsive to commercial immunoglobulin administration.

The patient was a 62-year-old man with diabetic and hypertensive nephropathies and a history of gout, who underwent cadaveric renal transplantation using pediatric-donor kidneys in an en bloc fashion in February, 1990. At the time of transplant, the recipient’s serologic titers were negative for hepatitis B surface antigen, anti–hepatitis B antibody, anticytomegalovirus IgM, and anti–human immunodeficiency virus antibody, while titers were positive for anticytomegalovirus IgG at 1:69, and for anticytomegalovirus IgG by ELISA. The donor was a 16-month-old girl who died of suspected cardiac arrest secondary to anoxia. She exhibited flu-like symptoms approximately 48 hr prior to the arrest. Donor serologic titers were negative for anti–cytomegalovirus, hepatitis, and human immunodeficiency virus antibodies. Parvovirus titers were not performed on donor or recipient sera, as they are not included in routine pretransplant serologic testing. The recipient was discharged 17 days posttransplant with a creatinine of 1.5 mg/dl and a hematocrit of 33.1% on an immunosuppressive regimen of FK506 (0.1 mg/kg b.i.d.) and prednisone (10 mg q.d.). He remained well until readmission one year posttransplant for an exacerbation of gouty arthritis affecting multiple joints, confirmed by fluid aspiration and treated by steroid injections and colchicine. At the time of admission, the patient was noted to be pancytopenic. Total WBC count was 1700/mm³, hematocrit 22.7%, platelet count 52,000, and reticulocyte count 0.1%, with normal red cell indices. Bone marrow aspiration and biopsy at that time revealed markedly decreased erythroid maturation with normal myeloid series and megakaryocytes, and increased iron stores (Fig. 1A). No viral inclusions were present. The serum anticytomegalovirus IgG titer was positive at 1:106 and the IgM titer was equivocal at 1:15. However, urine, throat swab, and buffy coat CMV cultures and the early antigen assay remained negative. Colchicine and prophylactic trimethoprim/sulfamethoxazole were discontinued as they were thought to be likely causes of the patient’s erythroid hypoplasia. His leukopenia and thrombocytopenia improved, and, following transfusion, the patient’s hematocrit stabilized at 27.7%. During the subsequent month, the patient received ten outpatient transfusions of packed red blood cells. He was readmitted one month after discharge with chest pain, and subsequently a myocardial infarction was excluded by enzyme and EKG criteria. At this second admission, his hematocrit was 21.6%, his total WBC count was 1700/mm³, his platelet count was 111,000, and his reticulocyte count was 0.1%. A peripheral blood smear revealed moderate microcytosis with rare anisocytosis and hypochromia. The serum erythropoietin level was elevated at 2820 mU/ml (normal 4–26). His chest pain resolved completely after transfusion of two units of packed red blood cells. Repeat cytomeg-

![Figure 1. Bone Marrow Morphology. (A) Bone marrow core biopsy on previous admission demonstrating erythroid hypoplasia. Myeloid cells and megakaryocytes are present. Intranuclear inclusions are not seen (H&E; X400). (B) Giant pronormoblast present in the marrow aspirate on second admission (Wright-Giemsa; X1000). (C) Bone marrow core biopsy on second admission illustrating numerous intranuclear inclusions (arrowheads) suggestive of viral infection. Infected cells are most likely red cell series precursors (H&E; X400).](image-url)
In the case reported here, the infant donor exhibited a viral prodrome prior to sudden death, and, since at least one case of death from myocarditis caused by parvovirus in an infant has been reported (1), this case raises the question of whether parvovirus B19 was transmitted from donor to recipient via the allograft. We retrieved autopsy specimens of myocardium and bone marrow from the infant donor in this case, both of which were tested by PCR and Southern-blot hybridization and found to be negative for parvovirus DNA. These tests do not, however, completely rule out the possibility of the presence of the virus in donor tissues. Further investigation into the prevalence of parvovirus B19 disease in transplant patients is warranted, as this infection may prove to be a common cause of anemia and aplastic crisis in the solid-organ transplant recipient.

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REFERENCES


Venoocclusive disease (VOD)* of the liver is a life-threatening bone marrow transplantation–related complication that may occur secondary to high doses of chemotherapy and radiation. VOD of the liver results from fibrous obliteration of the terminal hepatic venules, and involves jaundice, hepatomegaly, weight gain, and ascites (1, 2). The overall incidence of VOD after bone marrow transplantation ranges from 10 to 30%, with a mortality rate over 40%. The incidence of VOD varies according to the conditioning regimen; the incidence of VOD in patients administered cyclophosphamide (Cy) plus total-body irradiation (CyTBI) and busulfan (Bu) (4 mg/kg for 4 days) plus Cy (50 mg/kg for 4 days) (BuCy4) was 21–24% (3, 4), compared with 9% with BuCy2 (Cy 60 mg/kg for 2 days) (5). The pathogenesis is considered to be secondary to endothelial damage of the terminal hepatic venules, followed by activation of the coagulation cascade. More recently, it has been suggested that the dysregulation of cytokines such as tumor necrosis factor–alpha is implicated in transplant–related complications. It is also reported that serum TNF-alpha is increased prior to transplant–related complication such as acute graft- versus-host disease (aGVHD), interstitial pneumonitis (IP) and VOD (6, 7).

In two patients (one with chronic myelogenous leukemia, a 30-year-old man [case 1] and one with acute lymphoblastic leukemia L2, a 17-years-old boy [case 2]) jaundice, hepatomegaly, right upper abdominal pain, weight gain, ascites, and hepatic coma developed after allogeneic BMT using BuCy2 as a conditioning regimen and cyclosporine and methotrexate as immunosuppressants, respectively. Ultrasonographic studies of the abdomen revealed ascites, thickening of the gallbladder wall, and a failure to visualize the major hepatic veins. The diagnosis of VOD of the liver was confirmed from these clinical features. Both patients were treated with pulse therapy with methylprednisolone, continuous infusion of heparin as an anticoagulant, and prostaglandin E1 as a vasodilator. After intensive therapy, liver function of the patient with CML improved, ascites diminished within 10 days, and jaundice resolved within 30 days, and the patient was alive more than 4 months after transplantation without acute GVHD. On the other hand, although the liver function of the patient with ALL improved temporarily, it deteriorated from day 60 and the patient died of hepatic failure. Localized skin erosion of acute GVHD grade 1 was present from day 46 (Fig. 1). Autopsy of this patient revealed the typical pathological features of VOD, with fibrous obliteration of the terminal hepatic venules.

In the present study, we investigated the expression of TNF-alpha mRNA and IL-2 mRNA in peripheral mononuclear cells using the semiquantitative polymerase chain reaction (PCR) (8) to analyze the interaction of cytokines and VOD. The total RNA (5 μg) prepared from peripheral mononuclear cells separated by centrifugation with Ficoll-Hypaque gradient was reverse-transcribed by 600 U murine Moloney leukemia virus reverse transcriptase (BRL) with 150 pmol of random hexamer, and 1/6th of the resulting cDNA was used for PCR. The primers (IL-2A 5'CAACTCTCTTGCCTTTGAACTA3', IL-2B 5'AGTGACAAGCCTGTAGCCCATGTT3', TNF-alpha A 5'AGTGACAAGCCTGTAGCCCATGTT3', TNF-alpha B 5'AGCTCTCGAAAGTCGAGATAGTC3', beta-actin A 5'TTCGAGCAAGAGATGGCCACGGTC3', beta-actin B 5'AGCTCTCGAAAGTCGAGATAGTC3') were synthesized on a 380B DNA synthesizer (Applied Biosystems). The primer sequences were chosen from separate exons of the genes.

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* Abbreviations: Bu, busulfan; Cy, cyclophosphamide; PCR, polymerase chain reaction; VOD, venoocclusive disease.