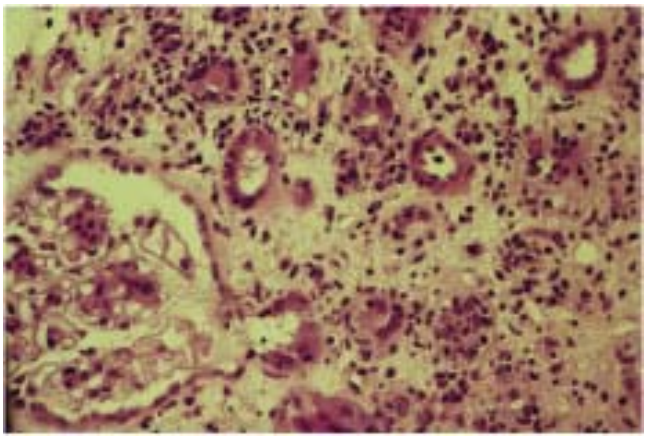
Case 8.1 Acute rejection

An 18-year-old student with end-stage renal failure due to chronic glomerulonephritis was given a cadaveric kidney transplant. He had been on maintenance haemodialysis for 2 months, and on antihypertensive therapy for several years. His major blood group was A and his tissue type was HLA-A1, -A9, -B8, -B40, -Cw1, -Cw3, -DR3, -DR7. The donor kidney was also blood group A and was matched for one HLA-DR antigen and four of six HLA-ABC antigens. He was given triple immunosuppressive therapy with ciclosporin, azathioprine and prednisolone.

He passed 5 L of urine on the second post-operative day and his urea and creatinine fell appreciably. However, on the seventh postoperative day, his graft became slightly tender, his serum creatinine increased and he had a mild pyrexia (37.8°C). A clinical diagnosis of acute rejection was confirmed by a finding of lymphocytic infiltration of the renal cortex on fine-needle aspiration. A 3-day course of intravenous methylprednisolone was started. Twenty-four hours later his creatinine had fallen and urine volume increased.

Subsequently, the patient had similar rejection episodes 5 and 7 weeks post-operatively. Both were treated with intravenous corticosteroids, and he has since remained well for over 3 years. Ciclosporin A was discontinued after 9 months but he still takes a daily maintenance dose of immunosuppressive drugs, namely 5 mg prednisolone and 50 mg azathioprine.



Case Figure 8.1 Acute rejection of human renal allograft showing histology with infiltration by lymphocytes and monocytes. Roitt & Rabson 2000.

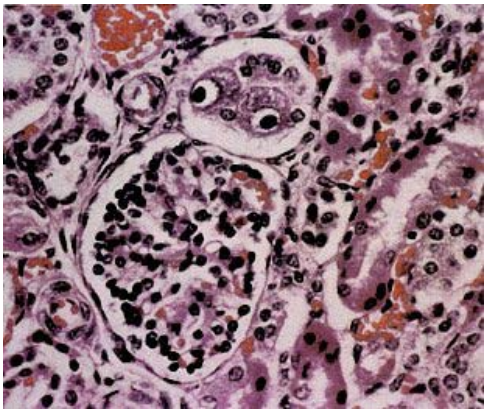
Essentials of Clinical Immunology, Sixth Edition. Helen Chapel, Mansel Haeney, Siraj Misbah, and Neil Snowden.

Case 8.2 Primary cytomegalovirus infection in a renal transplant recipient

A 22-year-old welder was given a cadaveric renal graft after a month of haemodialysis for end-stage renal failure. His immediate post-operative course was uneventful and he was discharged home on maintenance immunosuppressive therapy (ciclosporin A 5 mg/kg, prednisolone 30 mg and tacrolimus 0.20 mg/kg body weight daily).

He was readmitted on the 37th day with general malaise, muscle aches and fever but able to maintain a reasonable urine output (1700 ml/24 h). On examination, he had tender muscles and hepatomegaly; the transplanted kidney was not tender. Investigation showed a leucopenia but a normal serum creatinine.

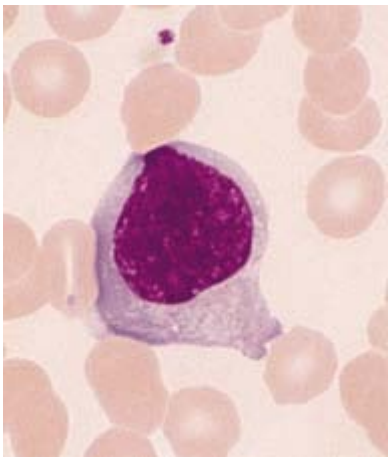
In view of the leucopenia, tacrolimus was withheld for 8 days, and intravenous corticosteroids were substituted. However, his serum creatinine began to rise and urine output fell, necessitating haemodialysis. Stored pre-transplant serum samples showed no evidence of anti-cytomegalovirus (CMV) antibodies or CMV antigen by polymerase chain reaction (PCR) analysis. However IgM anti-CMV antibodies were detected in a current serum sample accompanied by a positive PCR signal for CMV antigen. These findings indicated primary CMV infection in the recipient due to transplantation of a CMV-positive kidney into a CMV-negative recipient. He made a complete recovery following prompt treatment with a combination of ganciclovir (a CMV-specific drug) and CMV-specific immune globulin.



Case Figure 8.2 Characteristic owl's eye intranuclear inclusion bodies in the kidney of a patient with disseminated cytomegalovirus infection. Positive histology, as in this figure, is a very useful clue to the presence of CMV infection but serological confirmation should always be sought since production of antigen specific antibodies (IgG & IgM) are usually retained following transplantation. Reproduced with kind permission of Herriot R and Gray ES, New Engl J Med 1994;331:649.

Case 8.3 HSCT for acute myeloid leukaemia

A 22-year-old man was treated for acute myeloid leukaemia (AML) with cyclical combination chemotherapy, and complete clinical remission was obtained after three courses. However, remission in AML is generally short; half the patients relapse within a year and second remissions are difficult to achieve. Stem cell transplantation after high-dose chemoradiotherapy is therefore considered in young patients with suitable family members. The brother of this patient was HLA identical and willing to act as a marrow donor. The patient was given cyclophosphamide (120 mg/kg) followed by a dose of total body irradiation that is ordinarily lethal. Immediately after irradiation, he was given an intravenous transfusion of 10^9 unfractionated bone marrow cells per kg obtained from his brother. He was supported with granulocyte colony-stimulating factor and platelet transfusions during the days of aplasia before engraftment occurred. Methotrexate was administered intermittently to try to prevent GVHD. He was discharged home, well, 7 weeks after transplantation, and remains free of leukaemia 7 years later.



Case Figure 8.3 Peripheral white blood cells 'blast' from a patient with acute myeloid leukaemia; the blood film usually shows a hugely increased number of such blasts (up to 200x109/l) and few normal granulocytes.

Case 8.4 Graft-versus-host disease in an infant with severe combined immune deficiency

A 3-month-old boy was admitted to hospital with failure to thrive and a persistent cough. On examination his height and weight were below the third centile. Initial investigations revealed marked anaemia: Hb 50 g/l, white cell count 8.9×10^9/l, platelet count 260×10^9/l. A chest X-ray was reported to be compatible with right lower lobe pneumonia but no organism was identified on blood culture. He was treated empirically with broad-spectrum antibiotics but failed to improve.

In view of the anaemia he was transfused with two units of packed red cells (before the advent of irradiation policies for all blood/cellular blood products being irradiated before transfusion). Six days following transfusion he developed a widespread erythematous maculopapular rash and abnormal liver function tests. A skin biopsy showed diffuse vacuolar degeneration of basal epidermal cells with a mononuclear inflammatory cell infiltrate and aberrant expression of HLA-DR on epidermal keratinocytes. These findings were indicative of GVHD and raised the possibility of underlying immunodeficiency in the baby. Subsequent immunological investigations were diagnostic of SCID: i.e. marked T- and B-cell lymphopenia and hypogammaglobulinaemia.

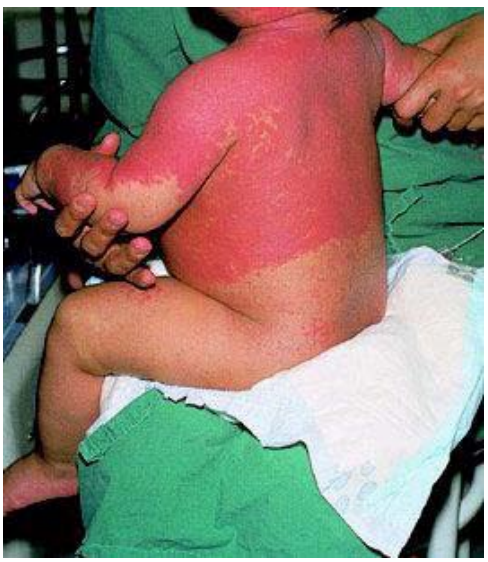
In the light of this diagnosis, the baby was bronchoscoped and analysis of bronchial secretions revealed Pneumocystis carinii, a common pathogen in babies with defective cellular immunity. The baby was treated aggressively with co-trimoxazole, intravenous immunoglobulin and prophylactic antifungal therapy. Despite his poor outlook, it was decided to perform a single haplotype matched stem cell transplant from his father. Sadly, this was unsuccessful and the baby died 3 days later from overwhelming sepsis. This was not unexpected, since transplantation in the face of established GVHD and sepsis often proves difficult. GVHD as a result of the use of non-irradiated blood should not occur now that there is greater awareness of SCID, but is included here to demonstrate the obvious similarity of findings between GVHD due to blood T lymphocytes and stem cells cells.

While the general principles of bone marrow transplantation for leukaemia and SCID are similar, comparison of this case with Case 8.3 highlights some important differences (Table 8.4).

Table 8.4 Comparison of bone marrow transplantation (BMT) for primary immune deficiency with BMT for myeloid leukaemia

	Primary immune deficiency	Leukaemia
Age	Infants and young children	Adults/children
Need for pretransplant conditioning	On theoretical grounds, not required but in practice some conditioning is beneficial	Yes
T-cell depletion of graft	Yes	Yes (but certain degree of GVHD is beneficial in view of its antileukaemia effect)
Complications (infections, GVHD)	Similar	Similar
Pace of immunological and haematological reconstitution	Similar	Similar

GVHD, Graft-versus-host disease.



Case Figure 8.4 Erythematous rash affecting the upper half of the body due to graft-versus-host disease (GVHD) in a baby with severe combined immunodeficiency. This is common after transfusion of non-irradiated blood (containing viable lymphocytes) or after non T depleted allogeneic bone marrow). Skin involvement in GVHD is often generalised. This Case Figure is exceptional in showing predominant involvement of one half of the body. Kind courtesy of Dr AJ Cant, Newcastle General Hospital.