To achieve sustained marrow engraftment the patient’s own immune cells must be eliminated or suppressed in order to allow donor-derived cells to replace the patient’s lymphohemopoietic system. Under controlled experimental conditions it is possible to distinguish between graft rejection due to a memory response following preceding sensitization, and failure of sustained engraftment in a nonsensitized recipient on the basis of genetic (hybrid, allogeneic) resistance. It is more difficult to separate these two mechanisms in man. Sometimes it is not certain whether a patient has been transfused or not, sometimes transfusions are given in the peri-transplant period, i.e. while the patient is receiving immunosuppressive therapy. Furthermore, factors other than allosensitization and resistance, e.g., defects of the microenvironment, can contribute to graft failure. In any event graft failure can manifest itself either as primary engraftment failure or as initial engraftment followed by secondary graft loss, generally within weeks, occasionally later. Graft failure may or may not be associated with reappearance of recipient cells, i.e. there may be cellular and occasionally humoral evidence of a host response to the attempted graft, or the graft may be lost for other reasons without there ever being an active host response. The latter certainly applies in patients given autologous grafts.

The definition of graft failure has been somewhat controversial. Generally, however, if a patient’s granulocyte count is not sustained at >200/µl by day 21 or, at the latest, day 28, graft failure is thought to be present. The diagnosis is further substantiated by biopsy findings of an empty marrow or low marrow cellularity without the presence of identifiable myeloid, erythroid or megakaryocytic precursors.

Some tests for documentation of donor cell engraftment are
Table 19. Documentation of donor cell engraftment

Cytogenetic analysis of metaphase spreads (Constitutive or after stimulation)
- Sex chromosome
- Autosomal chromosome marker
HLA Typing\(^a\)
- Serological
- Restriction fragment length polymorphism (RFLP)
- Sequence – specific oligonucleotide probes (SSOP)
Complement typing
Immunoglobulin allotyping
Erythrocyte typing\(^b\) – Antigens
- Enzymes

\(^a\) Especially helpful with HLA non-identical transplants; however, polymorphic DNA sequences outside HLA can be recognized by RFLP, SSOP or other probes.
\(^b\) Currently used only infrequently.

listed in Table 19. In some instances transplant recipients become “mixed chimeras”, a term referring to the fact that these patients carry normal lymphohemopoietic cells of donor and host origin. These cell mixtures may persist for years and possibly for the patient’s entire life.

The mechanisms involved in graft failure are incompletely understood; however, at least five categories can be distinguished:

a) In the presensitized patient given HLA identical un-manipulated marrow
b) In the patient transplanted with histoincompatible marrow
c) In the patient transplanted with T cell depleted marrow
d) In the patient transplanted with autologous marrow
e) In the patient with marrow defects.

The Presensitized Patient

Animal studies predicted that a transplant recipient given transfusions before transplantation would be at increased risk of rejecting a marrow graft even from a histocompatible donor. This was indeed the case in patients with aplastic anemia. Patients who had been multiply transfused before marrow trans-