Criteria for the Use of Irradiated Blood Products

Introduction

The infusion of immunocompetent lymphocytes into a recipient of impaired immunity may lead to engraftment of donor cells. The donor T lymphocytes engraft and mount an immunologic reaction against host histocompatibility antigens[7]. The subsequent graft-vs-host reaction could be fatal, in fact, the high mortality rate has lead to increased demands on transfusion services to supply blood products from which all mitotically active lymphocytes have been eliminated. Freezing and washing red cell units decrease, but do not totally eliminate viable lymphocytes. Irradiation has been used to eliminate the risk of graft-versus-host disease (GVHD) by inhibiting the proliferation of lymphocytes.

Clinically, GVHD is characterized by fever, liver function abnormality, profuse diarrhea and an erythematous skin rash. These symptoms can occur 3-30 days after the transfusion. Approximately 90% of patients with posttransfusion GVHD will die of acute complications, especially generalized infections. Treatment has included steroids, antithymocyte globulin, methotrexate and cyclosporine.

No study has comprehensively determined which patients are
susceptible to posttransfusion GVHD. Guidelines have emerged following cases reported in the literature. GVHD does not develop in healthy, immunologically normal individuals, nor has it been reported in patients lacking only humoral immunity (ie agammaglobulinemia). The susceptible host must lack the ability to reject the histoincompatible cells, the function of cell-mediated immune defenses.

Immune Deficiency Syndromes

Documented cases of posttransfusion GVHD in children has occurred in association with severe combined immunodeficiency syndrome (SCIDS)[10] and Wiskott-Aldrich Syndrome[4]. However GVHD has not been reported in patients with humoral immunocompetence alone (agammaglobulinemia) or diseases of neutrophil dysfunction (chronic granulomatous disease). Of eleven reported cases, the outcome of GVHD reaction was fatal in ten cases. There seems to be little controversy regarding the need for irradiated blood products in children with SCIDS, DiGeorge Syndrome or Wiskott-Aldrich Syndrome. The diagnosis for these patients rests with the clinician. Some would add erythroblastosis fetalis to the group of patients requiring irradiated blood products.

Bone Marrow Transplantation
Patients requiring bone marrow transplantation require irradiated products due to the ablative chemotherapy they undergo prior to the transplantation. There is no evidence that patients who will be transplanted at a later time, (2 weeks or more posttransfusion) require irradiated products. Although, lymphocytes are reported to survive beyond this length of time [8], it has been reported primarily in neonates who have received transfusions from their mothers. In the case of a patient requiring a red cell transfusion and requiring a bone marrow transplant in the future, there is no evidence that the lymphocytes will survive through the ablative chemotherapy and engraft. Therefore, a conservative recommendation may be to irradiate blood products given two weeks before anticipated bone marrow transplantation and up to three months after (until the bone marrow engrafts) and the patient can mount an immune response.

Although posttransfusion GVHD has not been reported in autologous bone marrow transplant patients, the real risk is unclear since these patients are, as are patients with allogenic bone marrow transplants, given almost entirely irradiated blood products. This seems reasonable since the preparative regimen of ablative chemotherapy and total body irradiation is similar to that given to recipients of allogenic bone marrow transplants.
Intrauterine Neonatal Exchange

Posttransfusion GVHD has been reported in four infants who had received intrauterine transfusions followed by exchange transfusions[5,11]. Also, GVHD was reported in three (premature and full term) infants[5]. The outcome in all these cases were fatal. By the small number of reported cases, it may seem that the incidence is low, however, as with all reporting, it is difficult to estimate what fraction of the total number of cases are reported. Fatal cases may be more easily recognized (and documented by autopsy), and therefore reported. Until this can be studied more extensively to evaluate the risk, it seems prudent to irradiate blood products provided for intrauterine neonatal exchange.

Hematologic Malignancies

Posttransfusion GVHD has been reported in patients with: acute leukemia[12] on intensive chemotherapy, especially in combination with radiation therapy, Hodgkin's disease[3] and nonhodgkins lymphoma. All the cases reported in lymphoma patients were fatal, however up to one third of patients with leukemia recovered. Efforts to evaluate the risk of GVHD in this population was estimated by one study as being between .1 and 1.0%[2]. In a large center, no cases of GVHD were documented in patients with acute leukemia who were transfused with non-irradiated blood, although
GVHD was reported among patients in the same center with Hodgkin's disease. It may be that patients with advanced lymphoma have a greater impairment of cellular immunity and are therefore at greater risk. With the absence of a large scale study in this area, it may be prudent to irradiate units given to patients with lymphoma. As the risk of GVHD appears to be smaller in the leukemic population, evaluation of the need for irradiated products may well be left up to the clinician caring for the patient.

Aplastic Anemia

The defect in aplastic anemia affects nonlymphoid cell lines and cellular immune functions are usually normal. The only report of GVHD in a patient with aplastic anemia is in a patient after an infusion of chronic myelogenous leukemia granulocytes; no cases have been reported secondary to normal-donor transfusions. Patients with aplastic anemia receiving antithymocyte globulin, (ATG), may theoretically be at increased risk during therapy-induced lymphopenia, although no cases have been reported. At the NIH, where large numbers of patients with aplastic anemia are treated, patients on ATG are given irradiated blood products (S. Leitman, personal communication).

Solid Tumors

Only two cases of GVHD have been reported in patients with
solid tumors: one each of neuroblastoma and glioblastoma. Although this would seem to imply a very low risk, the issue is clouded by the fact that some centers routinely irradiate all blood products given to patients with solid tumors. However, some centers, ie NIH (S. Leitman, personal communication) and UCLA (Pety, personal communication) do not consider patients with solid tumors to be indications for the use of irradiated blood products (with the exception of neuroblastoma) and have not seen GVHD in this patient population. Therefore it may well be that irradiated blood products are unnecessary in this patient population.

**Acquired Immune Deficiency Syndrome (AIDS)**

Despite the immunologic abnormalities (profound lymphopenia, altered T cell function, increased incidence of opportunistic infection, severe impairment of lymphocyte cell reactivity and cytotoxicity), no cases of GVHD has been reported in the AIDS population. At present, at least, the risk appears extremely low and irradiated products may not be needed in this group.

**Solid Organ Transplant Recipients**

Studies have not been done to evaluate the risk of GVHD in patients receiving heart, renal or liver transplants. Cases of
GVHD have not been reported in this patient population. Therefore, at present, there is little evidence that these patients require irradiated products, however, this needs to be more fully evaluated.
REFERENCES


