Gamma Irradiation:

Donor Blood and Blood Components.

Gamma Irradiation of Blood and Blood Components.

Why ?

Leukocyte Disarmament.

Gamma Irradiation of Blood and Blood Components.

Inevitably, leukocytes are present in blood components prepared by routine procedures, such as packed red cells (RBC) and platelet concentrate (PC).

A proportion of these leukocytes are T-lymphocytes, the effector cells that mediate TA-GvHD.

TA-GvHD

Transfusion-associated graft vs host disease.

A rare, but usually fatal complication.

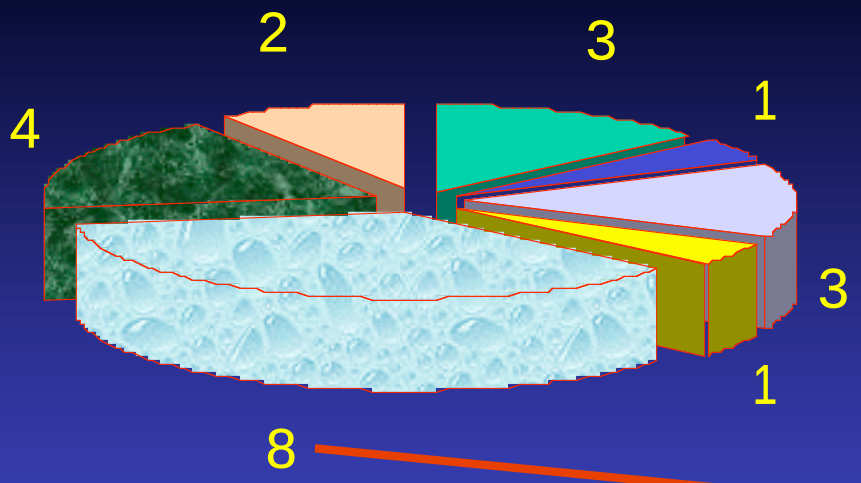
Mediated by viable donor lymphocytes.

Clinical manifestation 8-10 days post transfusion.

Risk is multi-factorial.

TA-GvHD

Transfusion-associated graft vs host disease.



Mortality Related to Transfusions

1996-1998 UK & Ireland

Williamson, L M; Lowe, S; Love, E M; Cohen, H; et. al.
Serious hazards of transfusion (SHOT) initiative: analysis of the first two annual reports.
BMJ, 319(7201).July 3, 1999. 16-19

Clinical indications for irradiation:

All directed donations from family members.

Shared human leukocyte antigen (HLA) haplotypes.

Clinical Indications for irradiation:

Patients with documented, suspected or potential immuno-deficiency disorders.

Congenital disorders.

Autologous bone marrow /peripheral stem cell recipients.

Allogeneic bone marrow transplantation.

Patients on purine analogue drugs.

Clinical Indications for irradiation:

Intrauterine transfusions (IUT).
Exchange transfusions (ET).

- Large volume transfusion.
- Immature recipient.

How much Gamma?

15 Gy ✗

20 Gy ✗

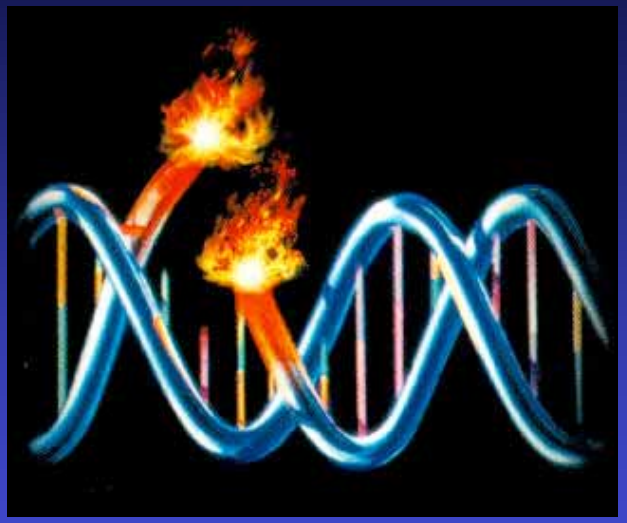
30 Gy ✓

1 Gy (Gray) = 100 rad

Mechanisms of Action.

Generation of free radicals within the leukocyte.

Damage to the DNA of nucleated cells.



Breaks induced in DNA strands.

The consequences of irradiation.

Increased potassium concentration.

Decreased intracellular ATP.

Decreased storage life.

Potential Hazards of Gamma.

Radiation induced malignant change.

Reactivation of latent viruses.

Leakage of plasticizer.

It may not work.

Photo-decontamination & Psoralens.

Group T cell dose x 10^6	Negative 0	Ta-GvHD 0.5	TA-GvHD 3.0	PCT 3.0	PCT 30
% Survival	88 7/8	11 1/9	22 2/9	100 5/5	100 9/9
Thymus cellularity	16.2 ± 0.8	7.2	< 0.1	17.1 ±2.4	16.3 ±3.3
Clinical Sign Day 38	0.6 ± 0.2	6.5 ± 2.5	6.1 ± 0.9	0.5 ± 0.2	0.3 ± 0.2
Skin Histology	0.16 ± 0.37	1.0 ± 1.0	1.0 ± 1.0	0.22 ± .41	0
Liver Histology	0.16 ± 0.37	1.7 ± 1.5	1.7 ± 1.5	0	0

Grass et al. Blood. 90:10 Suppl 1: 207a, 1997

Summary

All donor blood and blood products for immuno-compromised, suspected or potentially immuno-compromised patients should be irradiated.

There is no guarantee that it will work.

Alternatives are currently under clinical trial.