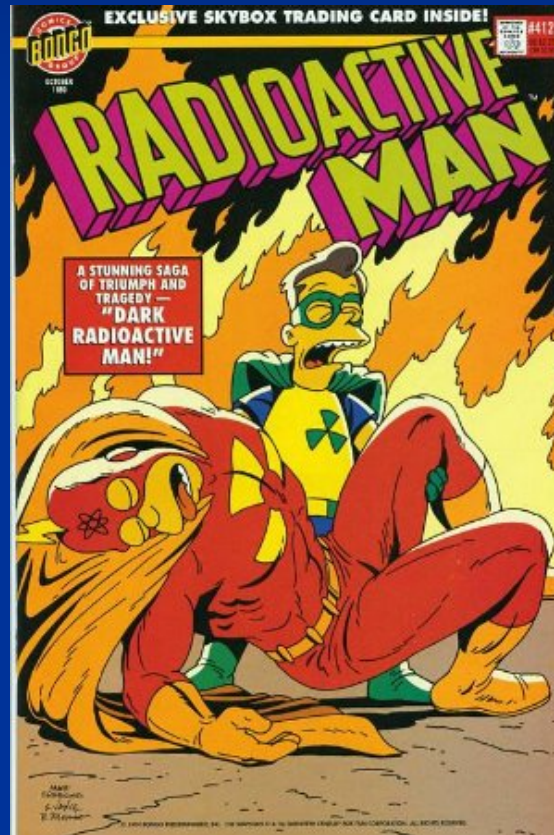


No Need to Go Gray Over Irradiated Blood Products

The New Proposed Guidelines Reviewed



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Outline

- TA-GVHD – Background
- Context of the Revised Guidelines
- New Recommendations and Proposed Changes
- Overview of Feedback Obtained
- Take Home Messages



What really happens when bitten by a radioactive spider...

Background

TA-GVHD - Pathogenesis

- Rare but serious complication of cellular blood component transfusion
 - All blood components containing viable lymphocytes can cause TA-GVHD
- Transfusion of immunocompetent T lymphocytes which engraft and proliferate in the recipient's bone marrow
 - Survival of these lymphocytes result from:
 - Shared HLA epitopes
 - Immunosuppression
- TA-GvHD presents clinically like GvHD associated with allo-BMT
 - Multisystem and cutaneous involvement
 - TA-GvHD is fulminant and rapidly fatal in the vast majority of cases
 - No real treatment options

TA-GVHD – Risk Factors:

- 3 significant factors appear to directly relate to increased risk of TA-GvHD including:
 - Susceptibility of the recipient's immune system to engraftment by donor lymphocytes
 - HLA homology between recipient and donor
 - Number of viable lymphocytes transfused

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"What is the Bloody Mary made with? A? B?
Rhesus negative? The menu doesn't say."

TA-GVHD – Preventative Strategies

- Appropriate utilisation of blood transfusions
- Irradiation of blood components
- Discourage directed transfusions and donations from HLA-selected/matched donors
- Institutional protocols to ensure recipients requiring irradiated components are identified
- Contentious Issues
 - ? Avoidance of transfusion of fresh blood
 - Universal leucodepletion?

Scope

- Guidelines cover:
 - Pathogenesis and pathophysiology of TA-GvHD
 - Procedural aspects
 - Equipment dosimetry and maintenance
 - Clinical indications for irradiated blood components
 - Future directions in preventing TA-GvHD

Context of Reviewing The Guidelines

- ANZSBT/ARCBS/NZBS Guidelines for Irradiation of Blood Components were last published in 2003
- BCSH are currently in review
- Expand/review previous guidelines
 - Provide evidence for recommendations, where available e.g. HSCT
- Collate and review the current literature

Preparation of the Guidelines



Preparation of the Guidelines

- Literature review
 - BUT the evidence is scant
 - Generally based on level III and IV evidence
- Consulted guidelines prepared by other professional and advisory bodies
- Attempted to acknowledge and address potential future methods for lymphocyte inactivation

Recommendations

Definitions:

■ Definite indications:

- These are indications where there is strong evidence to support the requirement for use of irradiated blood components or where there is clear consensus on the requirement within published guidelines

■ Possible indications:

- This includes settings where case reports have been published but where no controlled studies are available

■ No indication:

- No cases have been reported or insufficient evidence to mandate routine irradiation

Definite Indications

- Directed donations (from blood relatives)
- HLA-selected/matched platelet transfusions
- Granulocyte transfusions
- Intrauterine and all subsequent neonatal exchange transfusions
- Congenital cellular immunodeficiency disorders
- Allogeneic and autologous haematopoietic stem cell transplantation
- Hodgkin lymphoma
- Patients receiving purine analogues for malignant or non-malignant disorders

Possible Indications

- Premature infants and infants weighing less than 1300g
- All newborn infants
- Acute leukaemia
- Non-Hodgkin lymphoma
- Patients with B cell malignancy who receive non-nucleoside analogue-containing chemotherapy and/or radiotherapy leading to lymphopenia $<0.5 \times 10^9/L$
- T cell malignancies
- Therapeutic antibodies against T cells
- Patients receiving high doses of chemotherapy and/or irradiation sufficient to cause lymphopenia $<0.5 \times 10^9/L$
- Patients receiving long term or high dose steroids as therapy for malignancies
- Aplastic anaemia receiving immunosuppressive therapy
- Massive transfusion for trauma

No Indication

- HIV/AIDS (where none of the above apply)
- Congenital humoral deficiency disorders
- Solid organ transplantation (where none of the above apply)

Changes From Previous Guidelines

Definite Indications

- Aplastic anaemia
 - Placed in the possible indication section
 - Paucity of evidence in the literature regarding the association of TA-GvHD with aplastic anaemia
 - BUT many treatments used impair T-cell function
→ irradiated products should be considered - Not mandatory

Possible Indications:

- CML
 - No evidence of increased risk of TA-GvHD
- Non-Hodgkin lymphoma – All cases of B- and T-cell NHL now included
 - Case reports
 - SHOT data
- All newborn infants now included
 - No cogent evidence
 - BUT not always obvious whether a newborn has an immunodeficiency state
- Massive transfusion
 - Emerging evidence of chimerism in patients after massive transfusion
 - Significance is uncertain
 - No firm evidence for deleterious effects of chimerism currently exists

No Indication

- Thalassaemia and Haemophilia - removed
- Solid organ transplant – previously consider
 - No evidence to support routine recommendation for irradiated components in patients undergoing solid organ transplantation
 - Consider only if other clinical circumstances warranting irradiated components exist
- Term infants
 - Moved to the possible indications section

Summary of feedback

- Discrepancies between the revised Guidelines and BCSH Guidelines
- Request for definitive recommendations only
- Issue relating to difficulties with recommendations for neonates/paeds
 - Potential for delay in transfusion
 - Feasibility of more widespread use of irradiation in this cohort
- Issues regarding the potential provision of irradiated blood products in the massive transfusion setting
- Risk associated with evolving therapies in haematology and oncology and consequences of immunosuppression
- Duration of requirement for irradiated components

Take-home messages

- Limited evidence base
 - Many recommendations are expert opinions only
 - Case reports
 - No RCTs
- Guidelines \neq requirements
- Guidelines are for clinicians not lawyers
- Common sense must prevail
- Guidelines must be fluid and require constant revision
 - Development of new therapeutics affecting cellular immunity
 - As new evidence emerges and evolves

Thought of the Day

