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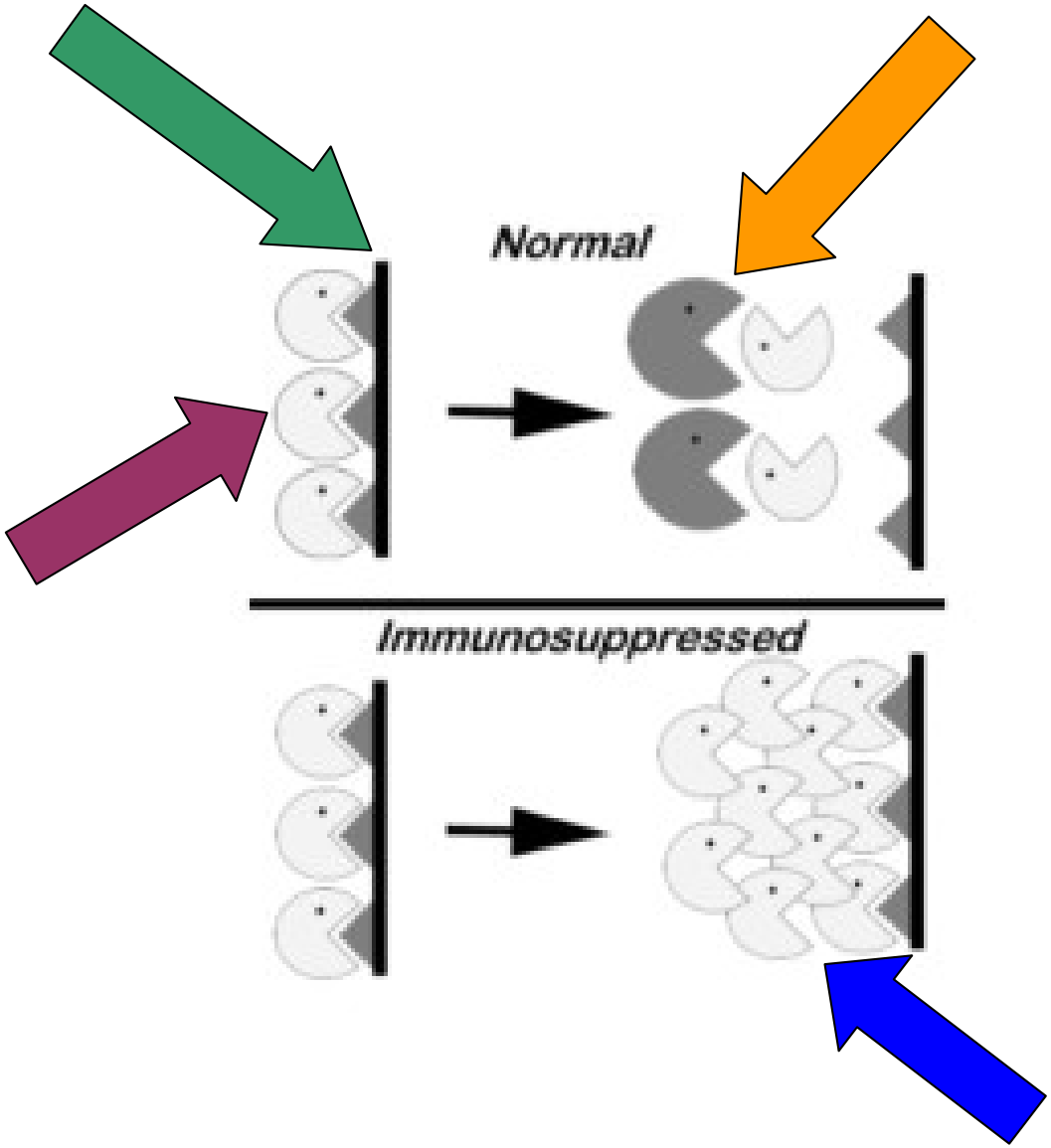
Please join in, take a guess, ask those ‘stupid’ questions...

Coming Up

- Why does blood need to be irradiated?
- Who needs irradiated products?
  - What happens if they get non-irradiated products?
- Whose responsibility is it anyway?

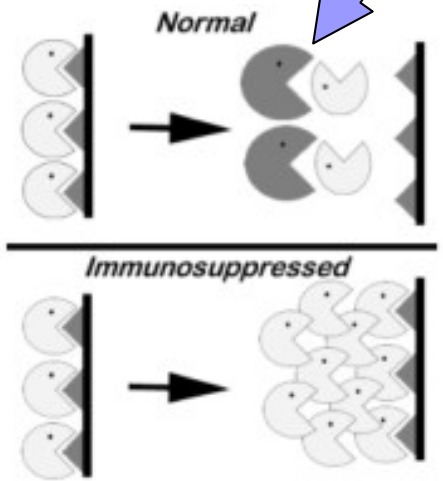
What condition are we trying to prevent when we irradiate?

Transfusion associated GVHD


Normal
Immunosuppressed

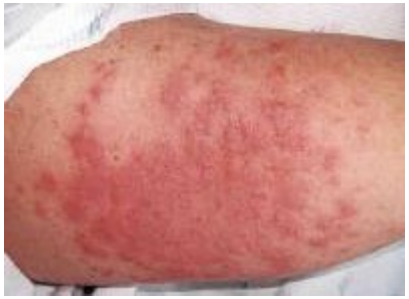
In immunocompetent patients: the recipient's own lymphocytes mount a counter attack, and being in the majority, will win.

Lymphocytes in the transfused blood 'look around' the body of the recipient and realise it is foreign to them – this puts them into attack mode.

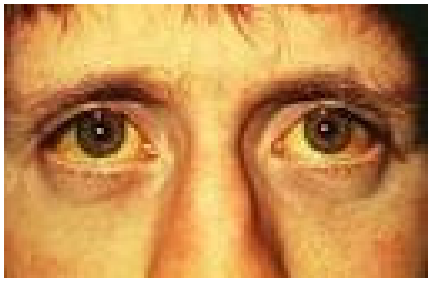


In immunocompromised patients: the recipient's own lymphocytes are absent or useless and thus the invading lymphocytes take over; the attack continues!

Manifestations of TaGVHD



Rash



Jaundice (liver inflammation)

Severe diarrhoea (gut inflammation)

Fever

Death (in 100%)

Irradiation prevents TaGVHD by...

stopping cell division.

Which products need irradiating?

YES

- Red cells
- Platelets
- Buffy coat/ granulocytes

NO

- FFP
- Cryoprecipitate
- PCC/factor etc
- IVIG
- Albumin

Irradiation is performed at blood centres using either gamma or x-ray sources.

So, who is at risk?

Haematology-Oncology practice:

- Hodgkins Lymphoma (lifelong)
- Fludarabine recipients (lifelong)
- Other purine analogues/antagonists (lifelong)
- Campath* (lifelong)
- Rabbit ATG** (lifelong?)
- Bone marrow transplant recipients.

A Case Study

- *A 21 week fetus scanned due to a history of maternal parvovirus infection.*
- *An urgent IUT was requested following signs of severe anaemia on ultrasound to allow the fetus to survive.*
- *The fetal medicine unit thought it was not possible to obtain red cells for IUT with less than 24 hrs notice to the Blood Service.*

Is this correct? What is your local experience?

Case Study continues

- *They transfused a total of 23 mL maternal blood to the fetus and the procedure was largely uneventful.*
- *The baby was delivered by emergency Caesarean section at 32 weeks gestation due to reduced fetal movements and was hydropic with pleural and pericardial effusions requiring chest drains and ventilation.*

What is wrong with the baby?

Case Study continues

- *The baby was pancytopenic at birth with Hb 50 g/L, neutrophils 0x10^9/L and platelets 9x10^9/L, and required multiple blood and platelet transfusions.*

What might cause this?

- *Parvovirus testing gave negative results.*
- *She developed conjugated hyperbilirubinaemia and evidence of a fungal chest infection.*

Case Study continues

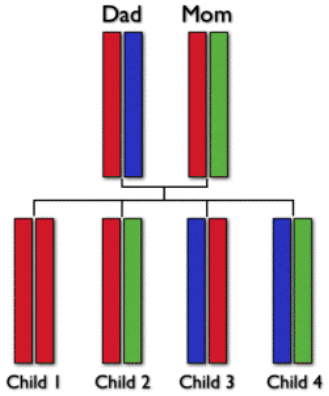
- *A bone marrow aspirate at 2 months of age confirmed that the pancytopenia was due to aplasia, and chimerism studies confirmed maternal engraftment.*
- *The mother was found to be human leucocyte antigen (HLA) homozygous. A diagnosis of TA-GvHD was made, and the baby underwent a stem cell transplant (maternal donor) but died of pneumonitis a week later.*

So what happened?

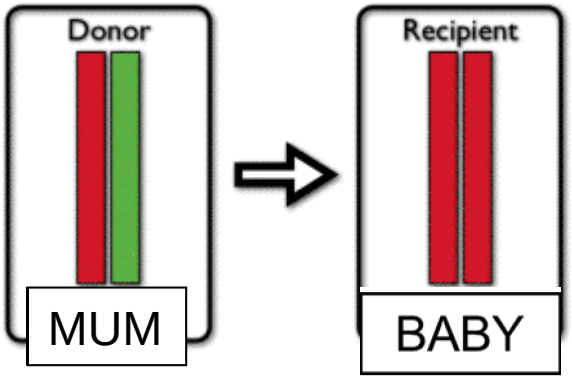
- A true case –SHOT report.
- Transfusions between family members are at risk for Ta-GVHD.
- First we need to understand…
- HLA – markers on cells which allow the immune system to recognise ‘self’ and ‘other’.
- Two copies carried by each of us – each half known as the haplotype.

Donations between family members

- By definition a mother and baby will share **one** HLA haplotype:

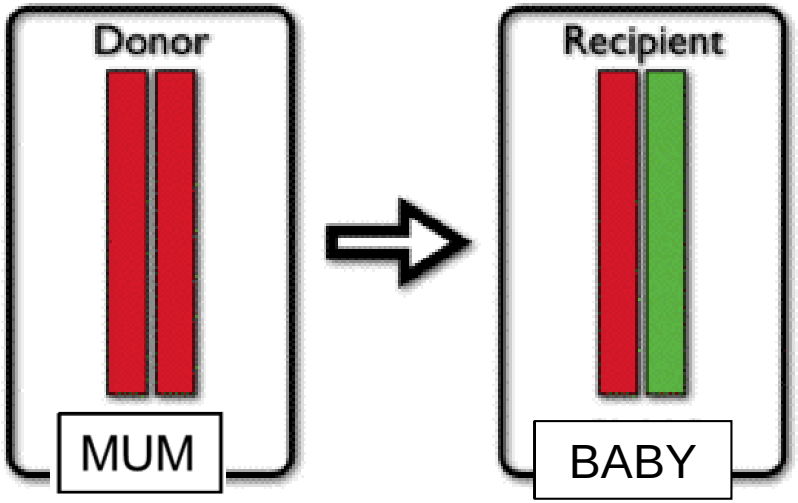


- In most cases they will share only one HLA haplotype. The remaining discrepancy is sufficient for baby to recognise mum as foreign and destroy mum's cells. (ie baby can 'see' mum's green in this image)



Donations between family members

- However, if the donor (mum) is HLA homozygous her cells will be ‘invisible’ to the recipient’s (baby’s) lymphocytes.
  - In this diagram Baby is unable to ‘see’ both red boxes as they already have the red haplotype. Thus baby’s immune system ignores mum’s lymphocytes.
- However the donor lymphocytes (from mum) *do* see the baby’s cells because they do not have the green haplotype in common.
- The donor cells start their attack without any response from baby.
- Thus an immunocompetent recipient can still develop GVHD.



- Theoretically there is always a risk that a donated product could do this to any patient if they had an HLA match (homozygote into heterozygote).
- However the chances of the necessary HLA combination occuring by chance between donor and recipient are miniscule.
- In addition research suggests the risk is higher in related HLA matched donor-recipient combinations, rather than in unrelated recipients.

Take Home Message

- Maternal to fetal transfusions are not safe!
  - Not irradiated
  - Not leucodepleted
- In an emergency it is safer to use donor pedipacks or neonatal-exchange packs that have not been irradiated than to use a directed donation.

Paediatric Indications for Irradiation

1. Immunodeficiency
    1. Severe T cell deficiency syndromes; these can be hard to identify but if there is concern irradiate until a diagnosis is reached.
    2. Congenital cardiac defects can be associated with immunodeficiencies – e.g. DiGeorge syndrome. If this is suspected irradiate, but cardiac defects are not an indication per se.
2. IUT +/- ET, either platelets or RBCs.

What does experience tell us in the IUT and ET population?

- The newborn, especially if premature, is at risk of TA-GvHD because of physiological immune incompetence.
  - Donor lymphocytes may be found in the neonatal circulation 6–8 weeks after exchange transfusion (ET)
  - Donor cells have been detected after IUT for HDN 2–4 years after transfusion in otherwise healthy newborns.

- Most cases of TA-GvHD reported in apparently immune competent infants have occurred in the setting of IUT followed by ET, suggesting transfusion-induced tolerance or immune suppression.

IUT and ET continued

Recommendations

1) IUT alone. Despite the few reported cases of TA-GvHD following IUT alone it is difficult not to recommend irradiation in the setting of a large-volume transfusion of fresh blood to a very immature recipient.

All blood for intrauterine transfusion (IUT) should be irradiated.

2) IUT followed by ET. Although reports are scarce, the published evidence supports a prudent policy of irradiation of blood for IUT and any subsequent ETs

Blood for neonatal exchange transfusion (ET) must be irradiated if there has been a previous IUT or if the donation comes from a first- or second-degree relative.

3) ET alone. Rare cases of TA-GvHD have been reported after ET alone in pre-term and term infants

For other neonatal ET cases, irradiation is recommended provided this does not unduly delay transfusion.

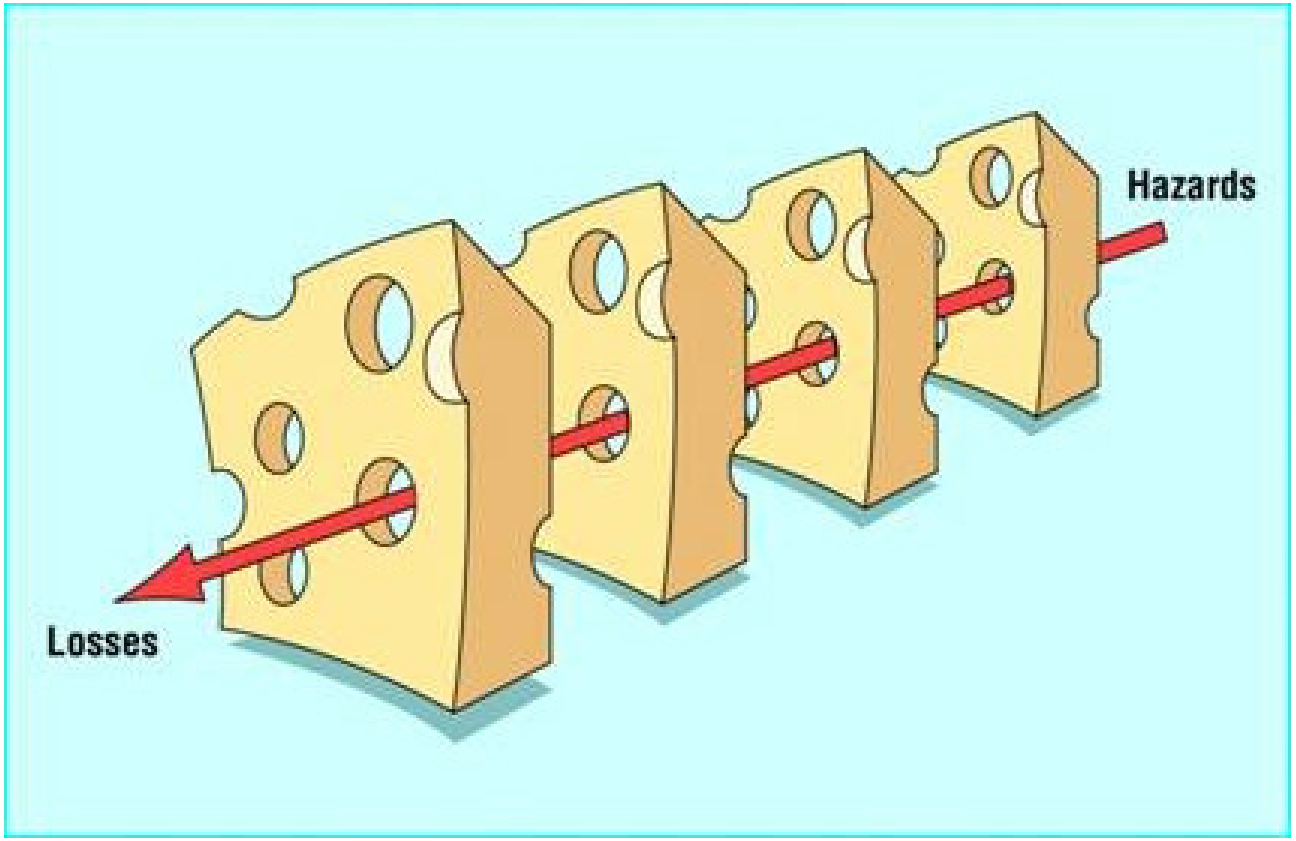
Who doesn’t need irradiated products?

- Top Up Transfusions
  - Neither premature nor term infants require irradiated blood products for top-ups, even multiple top ups.
- Routine cardiac patients.
- HIV/AIDS patients.

What a long list – why not zap the lot?

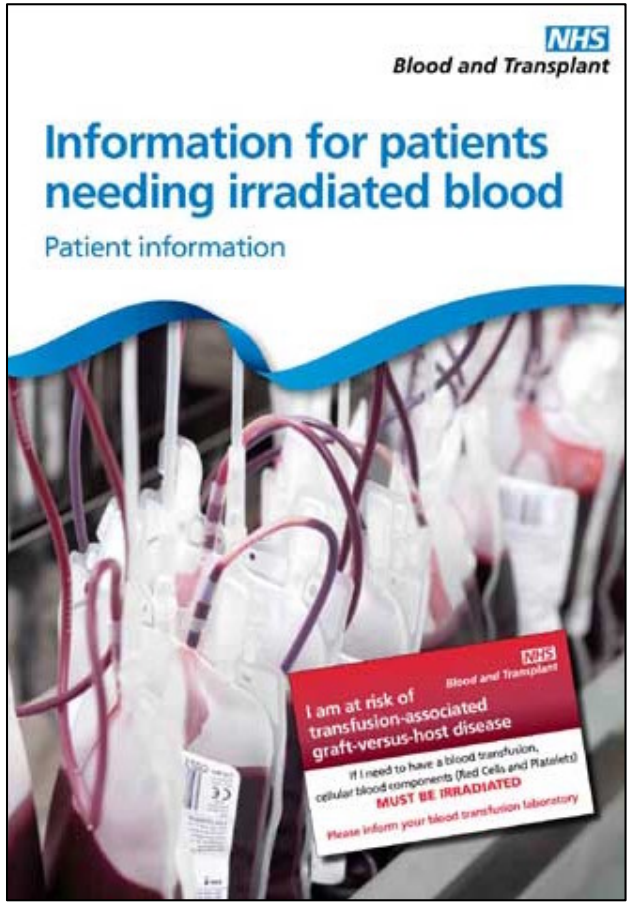
- Red cells become leaky after irradiation – potassium and free haemoglobin levels in the fluid increases.
- Therefore irradiated red cells can't be stored for as long as usual.
  - Must be less than 14 days old and then only stored for a maximum of 14 days, compared to usual red cell storage life of 35 days.
- And it's not cheap!

Whose responsibility is it anyway?



Who's responsibility is it anyway?

- Communication is a big problem
  - Consultant/SpR
  - Pathologist
  - Pharmacist
  - Blood bank
  - Transplant centres
  - Prescribers
  - Nurse
  - Patient?

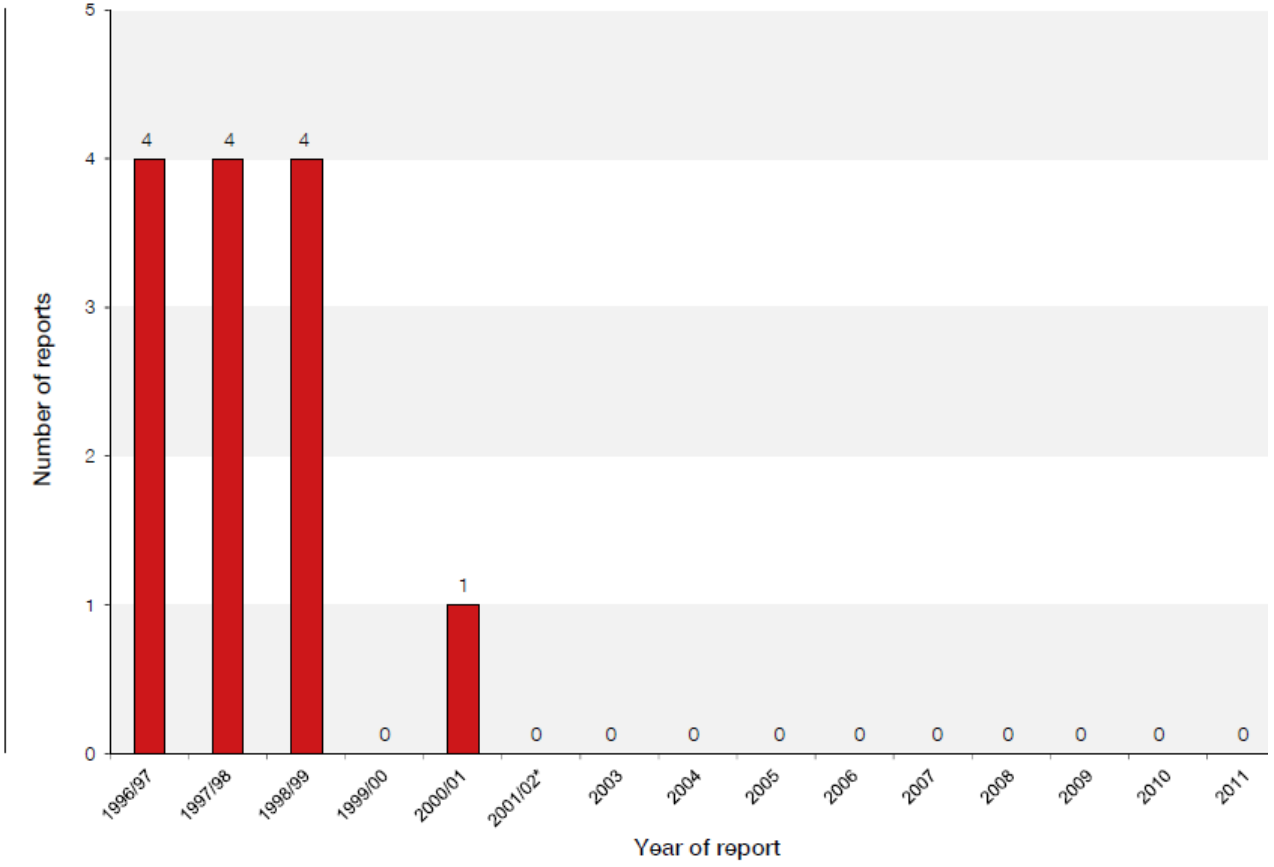


The good(ish) news…

- Universal leucodepletion was introduced in 1999.
- No cases of TaGVHD were reported between 2001 and 2012 (and only once since leucodepletion began, excepting current case)
- 877 cases of errors related to irradiated products reported to SHOT over this time.
- Leucodepletion may be enough to make blood is safe, but no-one is sure – so we can’t forget irradiation!

How are we doing?

Figure 20.1: Number of cases of TA-GvHD reported to SHOT each year



THANK YOU!

Questions?

Sources, references

- BCSH Guideline 2010 (www.bcshguielines.com)
- Haemovigilance: www.shotuk.org
- The blood bank guy (www.bbguy.org)