TRIM3ster

Can three pregnant women really be TRIM?

Responders vs Hyper-responders

- Alloimmunisation to blood group antigens is a major issue in transfusion.
- Around 1% of people exposed to red cells by transfusion or FMH will end up as a responder.
- Of this 1% of responders, 30% to 50% will go on to become Hyper-responders.
- 3 pregnant women KS (E, c, Jk^a), KR (c, S, Fy^a) and RH (K, Jk^b, Bg^b) have become hyper-responders during pregnancy.
- Is there any way that this can be prevented?
- Pregnant women, like non-pregnant hosts will react to immune stimulation in different ways.

TRIM

- Biological phenomenon with benefits for renal transplant patients and fatal consequences for cardiac patients.
- Broadly used term to explain transfusion complications mediated by proinflammatory or immunomodulatory pathways.
- Associated with changes in the immune system that include, but are not limited to:
  - Reduction in cell-mediated immunity
  - Changes in white blood cells
  - Decreased function in natural killer cells
  - Defective antigen presentation.
- Leucodepletion of RBC's has reduced the incidence.

Table 1 Postulated mechanisms of the TRIM effect.

- Clonal deletion of specific lines of immune cells
- Induction of suppressor T cells
- Production of anti-idiotypic antibodies
- Suppression of natural killer (NK) cell activity
- Polarization of the immune system to the T-helper type 2 responses, with suppression of T-helper type 1 responses
- Selection of non-responder type immune cells
- Mixed microchimerism
- Induction of apoptosis, resulting in the death of specific types of immune competent cells
- Accumulation in the supernatant of stored components of soluble molecules (e.g., histamine, eosinophil cationic protein,eosinophil protein X) that inhibit neutrophil function
- Accumulation in the supernatant of stored components of soluble molecules (i.e. soluble Fas ligand or soluble HLA class I molecules) that inhibit the immune response

Blood Reviews, Volume 21, Issue 6, 2007 327-348

Pregnancy and immunology

- Immune responsiveness of pregnant women being decreased was a theory that came from studies in the 1980's showing that immune responses to certain antigens is reduced.
- Then it was shown that there is little change in immune competence.
- It is now thought that immunomodulation of the mother is likely to exist during the pregnancy.
- All up, it has been muted that the overall immune response in pregnancy is related to non-rejection of the foetus (antigenicity incompatible).
- Current suggestions are that pregnancy uses innate inflammatory immune mechanisms to support the pregnancy.
- The placenta harnesses innate immunity processes to respond to stimuli.

PURPORTED ADVERSE EFFECTS OF TRANSFUSION-RELATED IMMUNOMODULATION

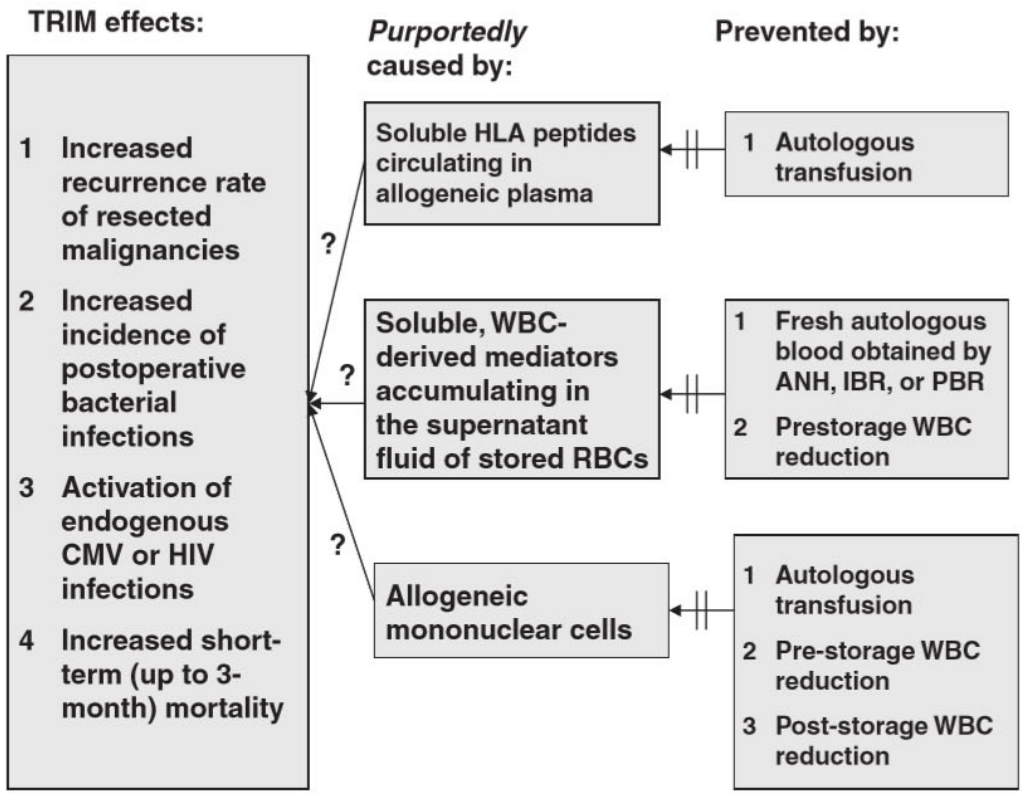

Fig 10.1 TRIM effects, postulated mediators of TRIM and preventive strategies that could be effective if the TRIM effects were mediated by each corresponding mediator. ANH, acute normovolemic hemodilution; IBR, intraoperative blood recovery; PBR, postoperative blood recovery. Modified with permission from Vamvakas EC. Deleterious effects of transfusion-related immunomodulation: fact or fiction? Update through 2005. *Am J Clin Pathol* 2006; 126 (Suppl 1): S71–S85.

Questions

- What if any red cell antigens are subject to TRIM?
- Is there a case for prophylaxis other than Rh(D) Ig?
- Do chemokines aid or detract from the process?
- Where antibodies are formed due too trauma in pregnancy, is there the same mechanism occurring here, as it does in actual trauma cases?
- What does the further hold for pregnant hyper-responders and their babies?
- Have we any evidence that TRIM can be beneficial in red cell antigens transfers across the placenta?
- Will clinical trials ever be carried out?
- What direction (if any) will the future research into immunomodulation in pregnancy lead us?

References

- Daniels G, Poole J, deSilva M et al. The clinical significance of blood group antibodies. Transfus. Med. 12(5), 287–295 (2002).
- Blood Reviews, Volume 21, Issue 6, 2007.
- Transfusion-related immunomodulation: a reappraisal Current Opinion in Hematology: November 2017 - Volume 24 - Issue 6.
- Transfusion Medicine Neil Blumberg, Joanna Heal 2007.
- American Journal of Transplantation 2013; 13: 229–231 Wiley Periodicals Inc.
- Immunomodulation in transfused trauma patients. Curr Opin Anaesthesiol . 2013 April ; 26(2)
- Mechanism of human chorionic gonadotrophinmediated immunomodulation in pregnancy Expert Rev. Clin. Immunol. 8(8), 747–753 (2012)

References

- Solving the dilemma of prevention of red cell alloimmunization Stephen J, Cairns LS, Pickford WJ, Vickers MA, Urbaniak SJ, Barker RN. Identification, immunomodulatory activity and immunogenicity of the major helper T cell epitope on the K blood group antigen. Blood 119(23), 5563–5574 (2012).
- Immunomodulation and immunotherapy: Drugs, cytokines, cytokine receptors, and antibodies Robert P. Nelson, Jr, MD,a and Mark Ballow, MDb Indianapolis, Ind, and Buffalo, NY
- Frequency and Specificity of Red Blood Cell Alloimmunization in Chilean Transfused Patients Transfus Med Hemother 2015;42:4–7
- Alloimmunization in multitransfused liver disease patients: Impact of underlying disease Asian J Transfus Sci. 2016 Jul-Dec; 10(2)