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Is Partial matching of blood group antigens a mitigation strategy to reduce alloimmunization

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Introduction

- **Alloimmunization is the immune response evoked in an immuno-competent host with the introduction of an incompatible antigen**
- **Detection of alloimmunization became possible only with introduction of ICT by Coombs in 1945**
- **Sources of alloantibody formation**
  - ✓ **Transfusion**
  - ✓ **Pregnancy**
  - ✓ **Transplantation**
  - ✓ **Injections of immunogenic materials or IVIg / RhIg (passively acquired)**
- **RBC alloimmunization considered if Hb < 9.0-9.5 gm % or significantly less than usual for a particular patient prior to transfusion on 2 occasions.**

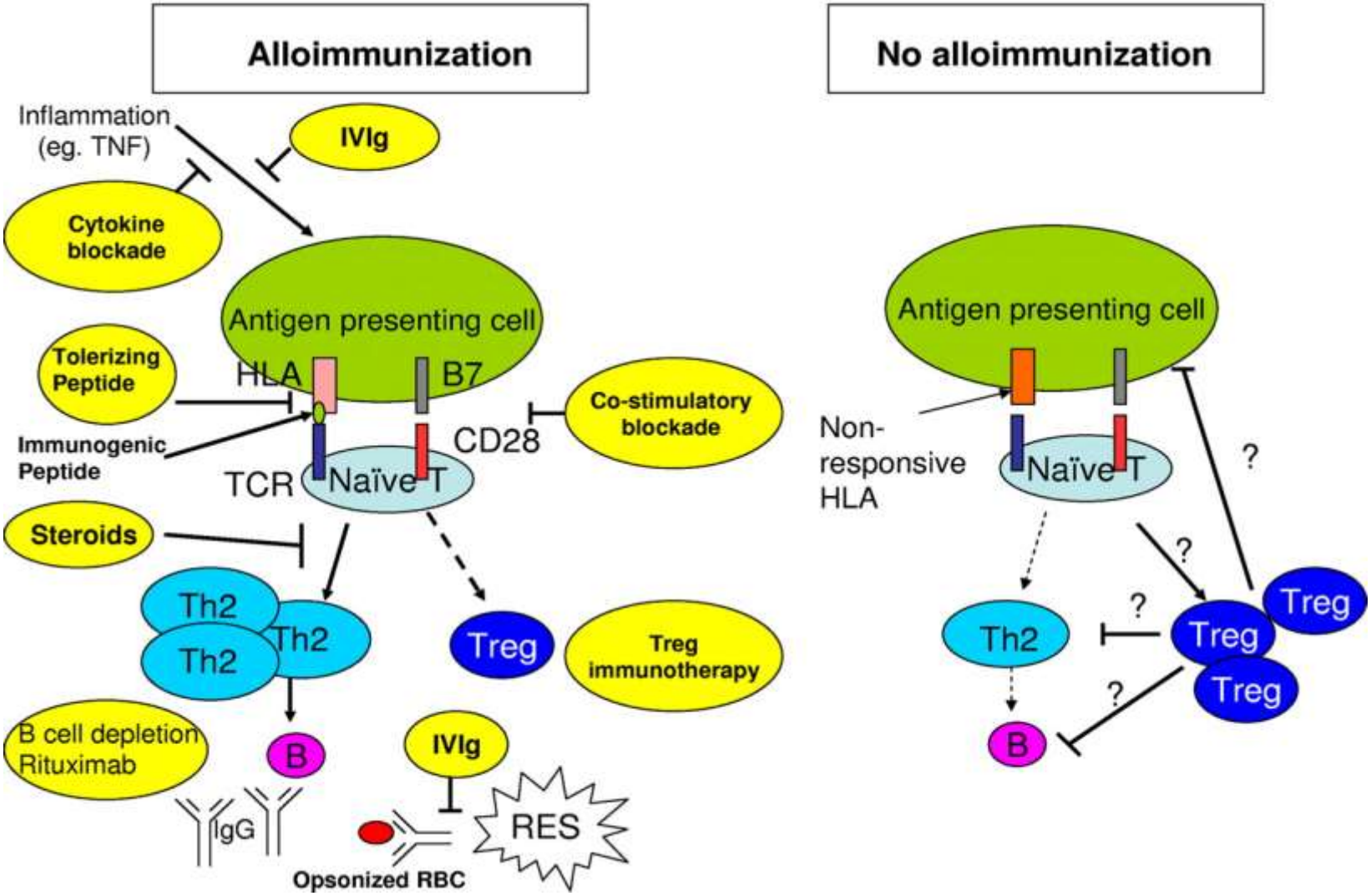
Factors influencing alloimmunization

- Genetic factor: genetic disparity between patient & donor RBC
- Immunogenicity of antigen
- Chemical & physical form of antigen
- Number of antigen sites
- Degradability of antigen
- T-cell response of patient
- Disease's pathophysiology of pt.
- Intensive immuno-suppressive therapy
- Age & gender of patient
- Immunomodulatory effect of allogeneic blood on pt. immune system

Post Tx antibody frequencies

- General pt. population : 1- 3%
- Multi transfused pt.: upto 70%

RBC alloimmunizaton pathobiology



Alloantibodies

1. Rh system antibodies: D C E c e
2. Kell system antibodies: K
3. Duffy system antibodies: Fya & Fyb
4. Kidd system antibodies: Jka & Jkb
5. MNSs system antibodies: S & s

Clinically significant

1. Lewis system: Lea & Leb
2. MNSs system: M & N
3. P system: P1

- React at cold temp (IgM)
- Not clinically significant
- Anti-M may react at 37° C

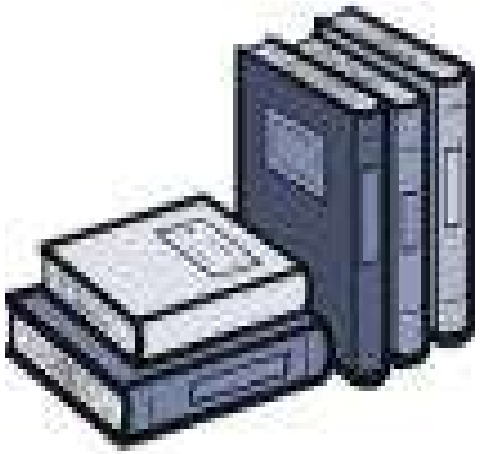
Relative immunogenicity: D>K>c>E>k>e>Fya>C>Jka>S>Jkb

Clinically Significant Alloantibody

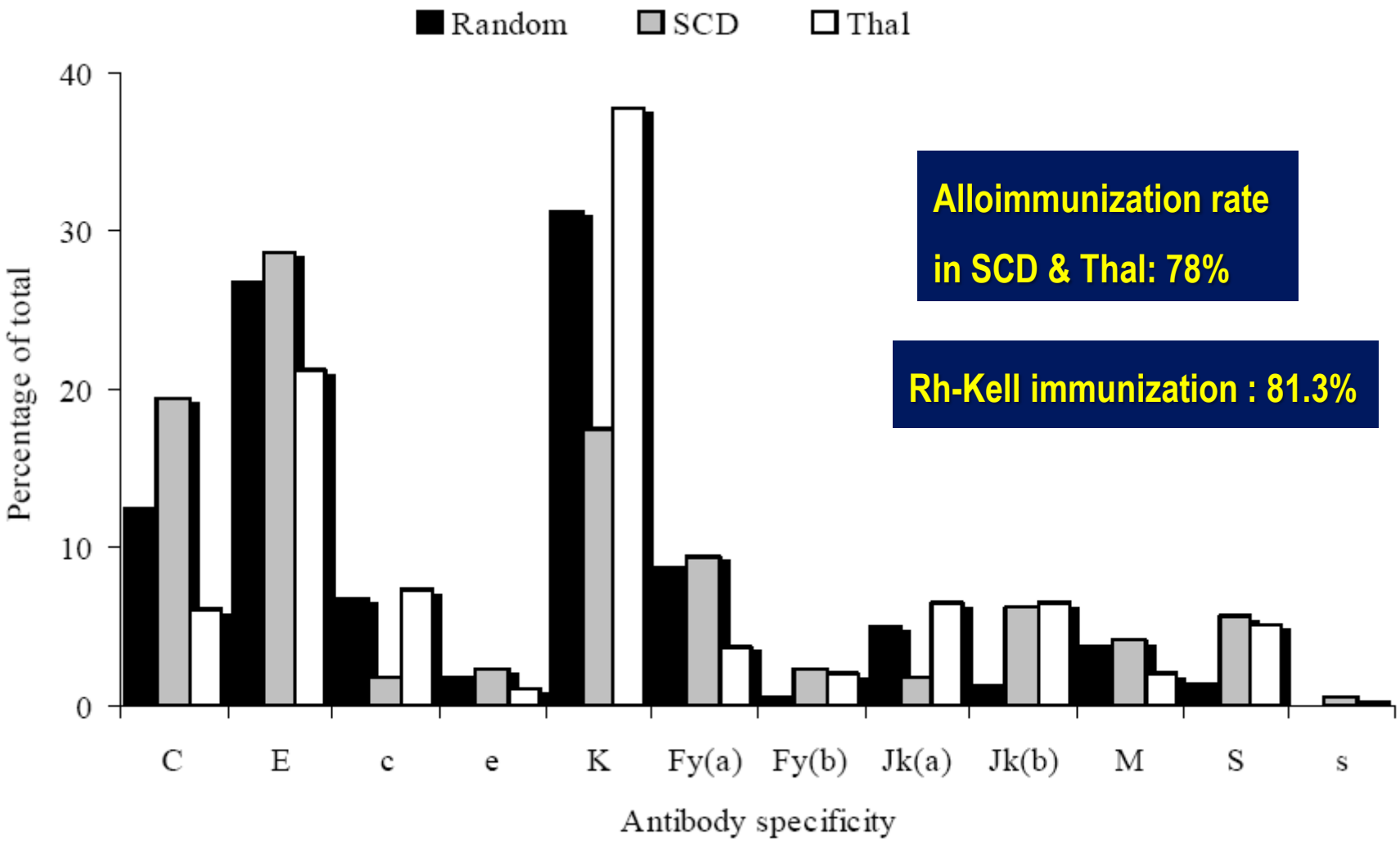
- IgG type & react at 37° C
- Cause hemolytic transfusion reactions
- Cause marked decrease in survival of transfused red cells
  - ✓ Anemia & Jaundice
  - ✓ Frequent blood Tx
- Causes hemolytic disease of the fetus or newborn

- Anti-K is produced in 10% of incompatibilities, anti-E in 7%, anti-c in 3%.
- Immunogenicity of the other specificities is so low that antibodies are only produced in less than 3% of incompatibilities.

Review of Literature



Total of non-D 10226 antibodies in multiply transfused patient over a study period of 20 years (3 centers). Winters et al Transfusion 2001



Alloimmunization rate in SCD & Thal: 78%

Rh-Kell immunization : 81.3%

Singer et al. Department of Hematology/Oncology at the Children's Hospital Oakland, California, USA .*Blood 2000*

- 64 transfused thalassemia patients evaluated.
- 14 (22%) developed alloantibody, 77,3 % immunized to K, c, E and Fyb
- Tx of Rh & Kell matched blood effective in preventing alloimmunization

Frequency of irregular red cell alloantibodies in patients with thalassemia major: a bicenter study. *J Pak Med Assoc 2005*

- 97 patients were included in 1 yr period
- Alloantibodies found in 9 (9.2%)
- 3 (33.3%) developed anti-K while 2 (22.2%) had anti-D

Frequency of red cell alloimmunization in patients with sickle cell anemia in an Egyptian referral hospital. EJH 2012

- Of 42 SCA patients 9 developed alloAb. Anti-K, anti-E,anti-C in 69.5%
- **Suggestion:** Regular Ab screening & Rh-Kell matched blood Tx

Indian studies

Red cell alloimmunization in a transfused patient population: a study from a tertiary care hospital in north India (PGIMER). IJMR 2009

- overall incidence of alloimmunization was 3.4% (18/531)
- Anti-c most common specificity (38.8%), followed by anti-E (22.2%), anti-M (11.1%), anti-Le(a) (11.1%)
- ***Conclusion:*** Pre-transfusion antibody screening on pts samples prior to crossmatching needs to be initiated in India to ensure safe transfusion

Red cell alloimmunization in multi-transfused chronic renal failure patients undergoing hemodialysis. SGPGIMS. Indian J of Hemat 2000

- RBC alloimmunization rate 9.8% (8/81). 9 alloantibodies detected in 8 patients, 88% involving Rhesus & Kell systems. Rh-Kell matching Tx suggested for prevention

Indian studies

Alloimmunization to red cells in thalassemics: emerging problem and future strategies. New Delhi. Trans & apher Sci 2011

- **Red cell alloantibodies found in 9.48%**
- **Most common antibody was Anti-E (36.4%) followed by Anti-K (27.2%)**

Conclusion: **Institution of Rh & Kell phenotyping followed by provision of matched blood prevent alloimmunization**

Alloimmunization & red cell autoimmunization in multi transfused thal of Indian origin. Lady Hardinge Med College. Hematology 2010

- **Alloimmunization 3.79% (80% Rh & K) & autoimmunization 0.47%**

Advice: **Need to formulate balanced & cost-effective approach for Tx management of thal to minimize alloimmunization & autoimmunization.**

Blood Transfusion Strategy in multitransfused patient

Receipt of sample & requisition

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Confirm blood group

↓

Antibody screening using 3-cell panel

Negative ↓

Positive ↓

Antibody identification using 11-cell panel

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Correspondent antigen negative blood

←

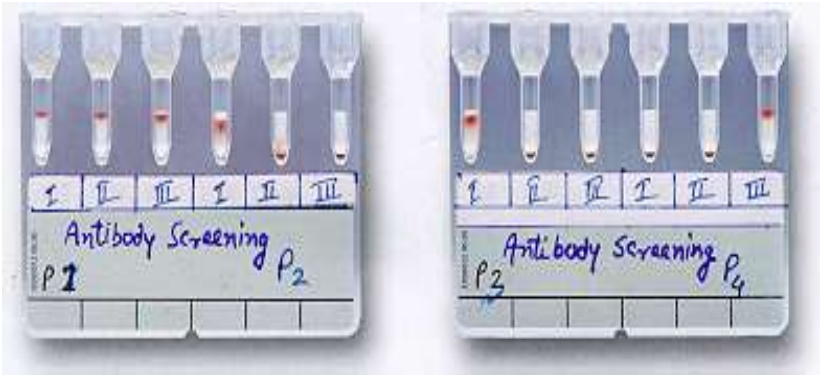
Coombs crossmatch

↓

Issue Rh & Kell matched compatible blood

↓

Documentation



Preventing alloimmunization

- Extended red cell phenotyping at diagnosis is always preferred
- In resource poor setting / countries with economy constraints

at least Rh & Kell phenotype (partial phenotype) may be advised

- Partial matched, leuko-reduced blood Tx may be implemented
- Optimization of Tx interval
- Prevent lot of Tx side effect in patients
- Pool of designated donors (directed donation)

Recent advances & future strategies

- Prevention of alloimmunization through immunomodulatory therapies
  - ✓ Immune cell depleting agents
  - ✓ Costimulatory blockade (T cell-B cell interaction)
  - ✓ Cytokine blockade
- Down regulation of lymphocyte activation
- Induction of tolerance through immunodominant peptides

Animal trials are on

Summary

- Preventing alloimmunization as well as managing alloimmunized multitransfused patient is challenge to both clinicians & blood bank
- Alloimmunization preventation should be the goal
- Partial red cell phenotyping at diagnosis should be adviced
- All blood bank should be well equipped to detect antibody, perform proper crossmatching & issue appropriate blood
- Tx of partially matched blood (Rh & Kell matched) definitely reduces alloimmunization.

Thank You

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