Performance Appraisal of HLA Antibodies in HSCT

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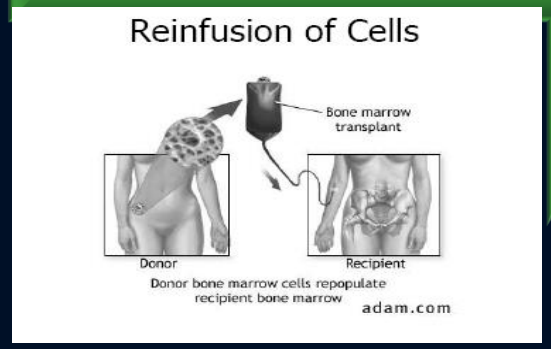
Relationship……

Transfusionests



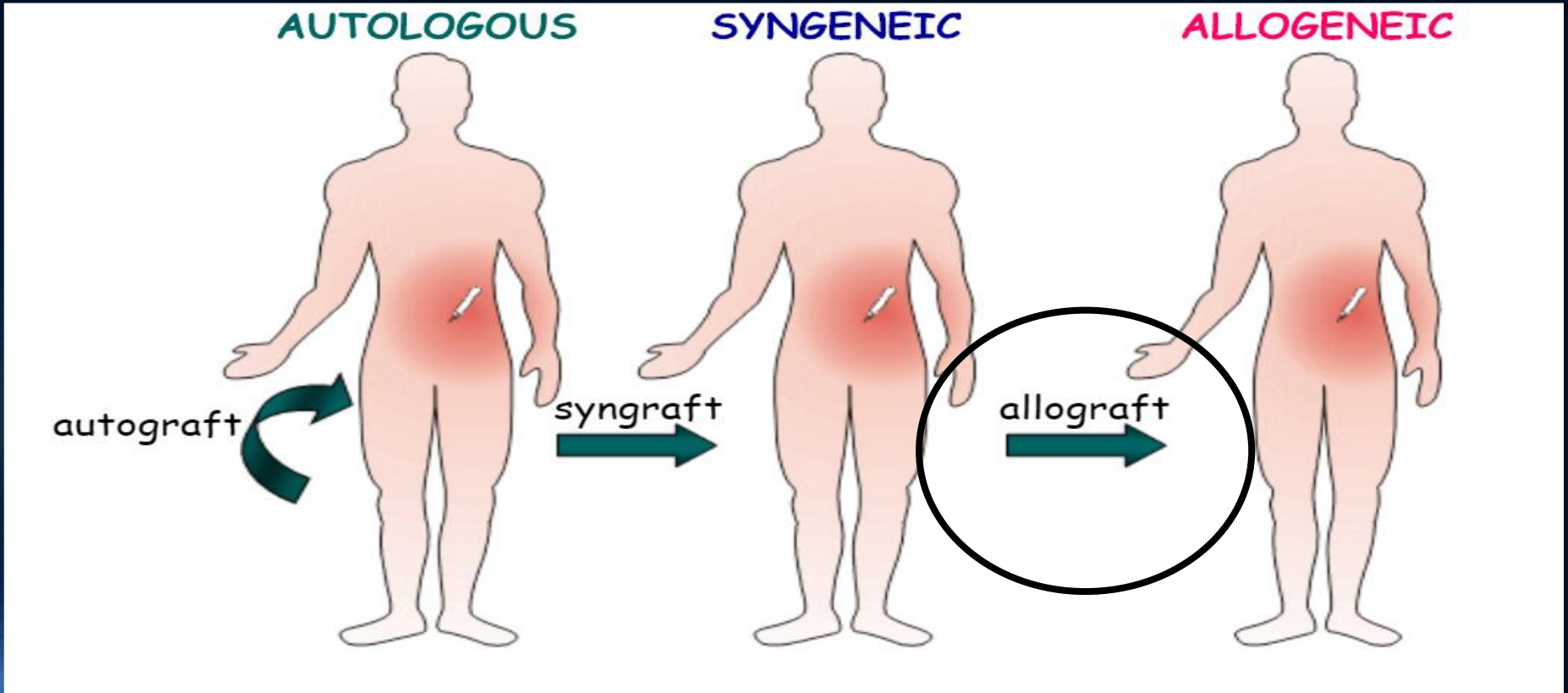
Transplanters

Performance Appraisal

Retrospective Evaluation → Opportunity to change → Appraise the contribution

Tissue/ Solid organ transplantation

- The success of transplantation and maintenance of donor tissue/ cells depends majorly on Histocompatibility



Full HLA Match

HLA Mismatch

GVHD

Stem Cell Transplant Process Scheme

- Full Match Sibling
- Saudi Stem cell Registry (MUD)
- Haplo-identical donor (50% Match)
- International Stem cell Registry
- Cord Blood Unit

Like hood of finding identical sibling in Saudi population ~62%

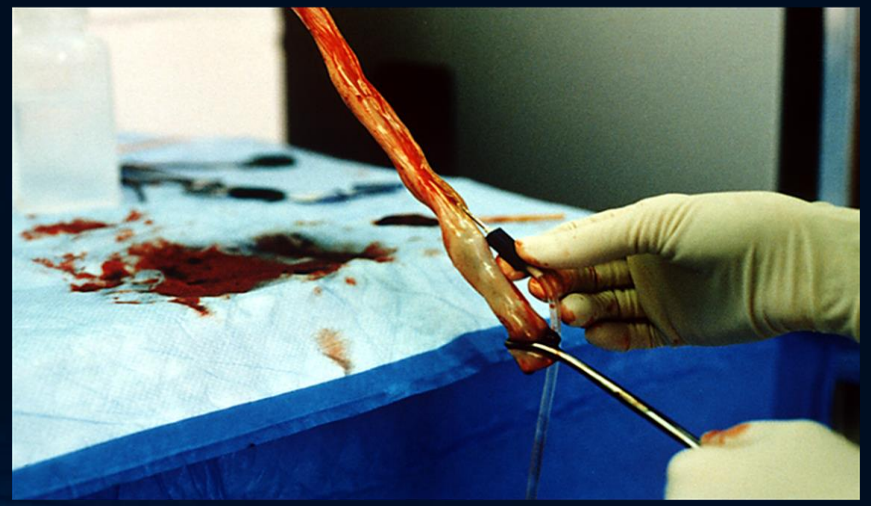
38% No full match donor

New Opportunities

Cord Blood Transplant

- GVHD Diminished
- Relax HLA matching

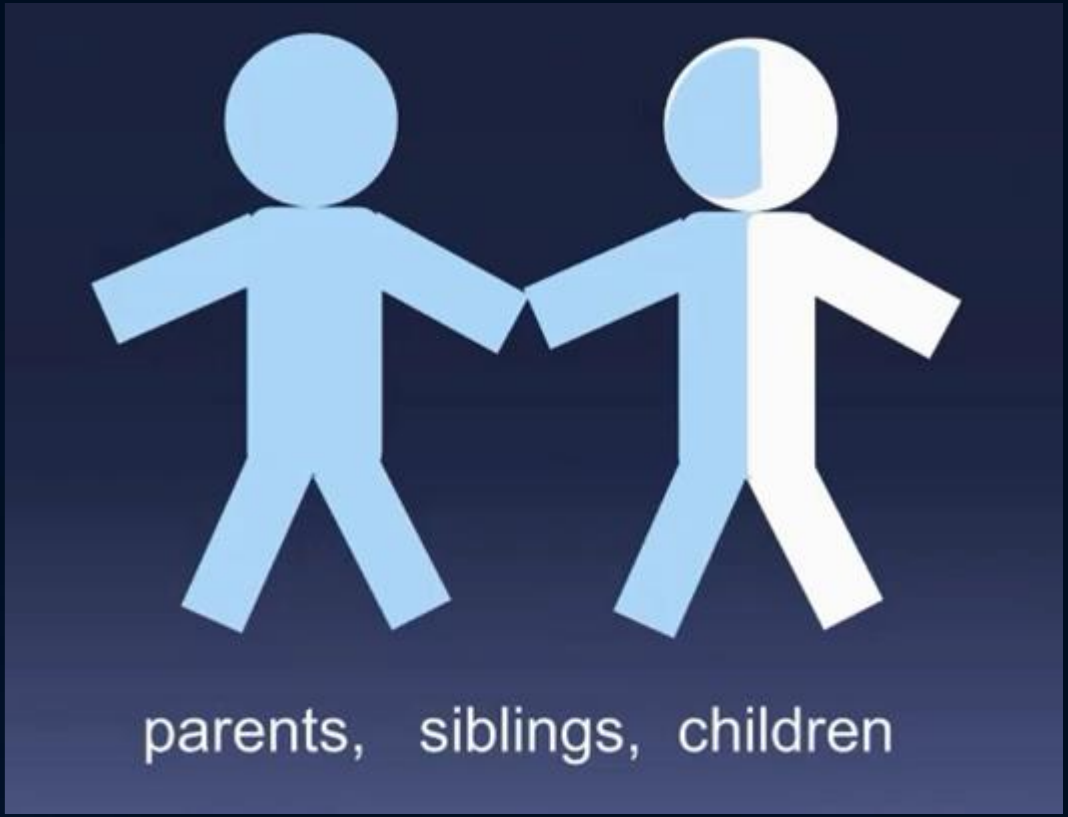
- Graft Failure
- CD34



New opportunities

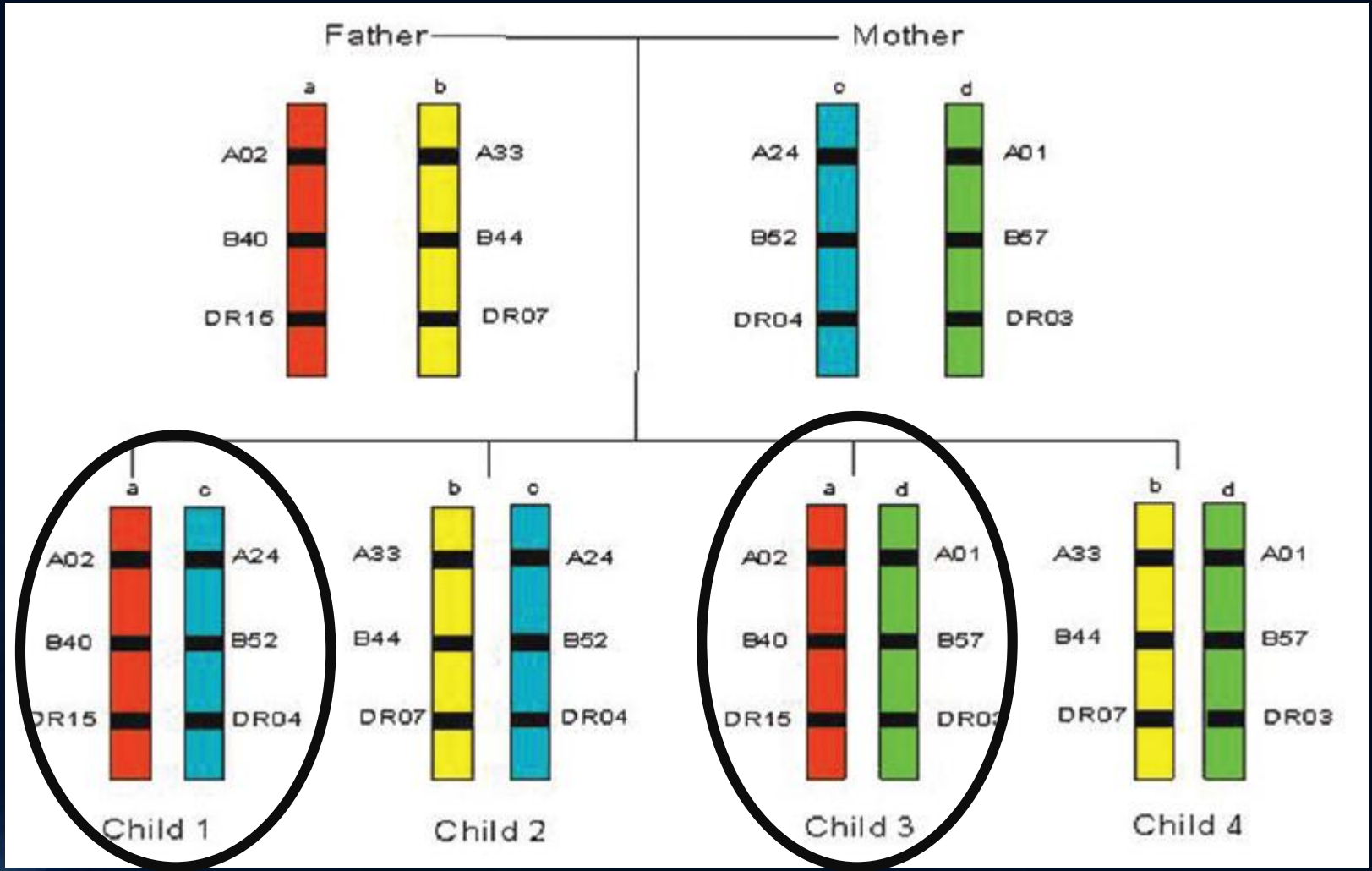
Selection of an unrelated HLA matched donor is very difficult

New opportunities



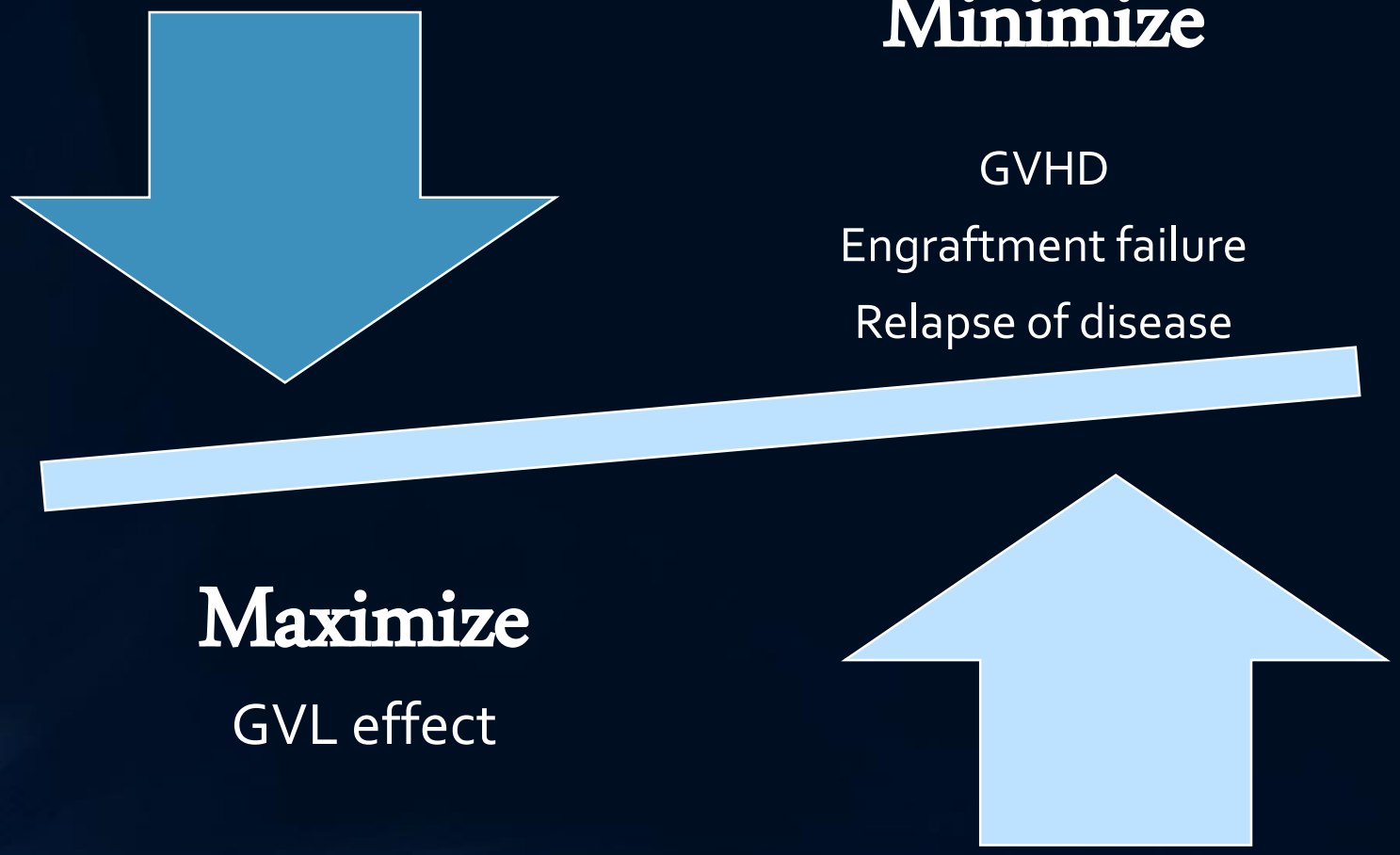
New opportunities Like hood of finding Haplo-identical in Saudi 94%

Haplo-Identical SCT



50% HLA match

Balance in SCT



HLA antibodies " New Barriers"

Induce

HLA Antibodies

Association to Causation

Strength

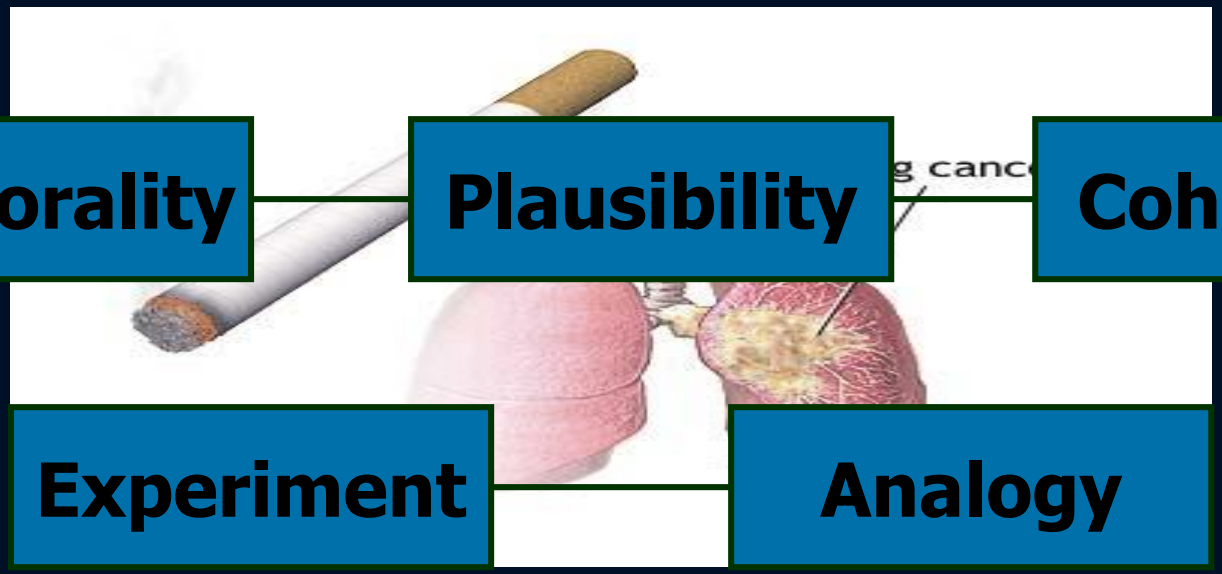
Consistency

Specificity

Temporality

Plausibility

Coherence



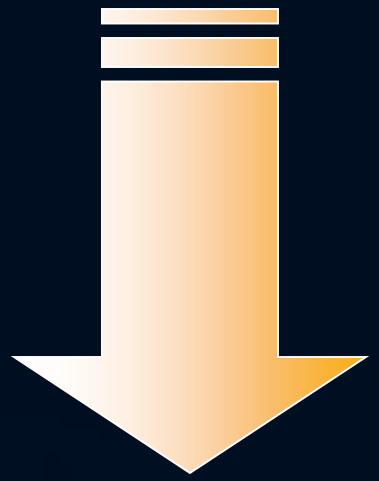
Experiment

Analogy

Biological Gradient

Association to Causation

Anti HLA Antibody

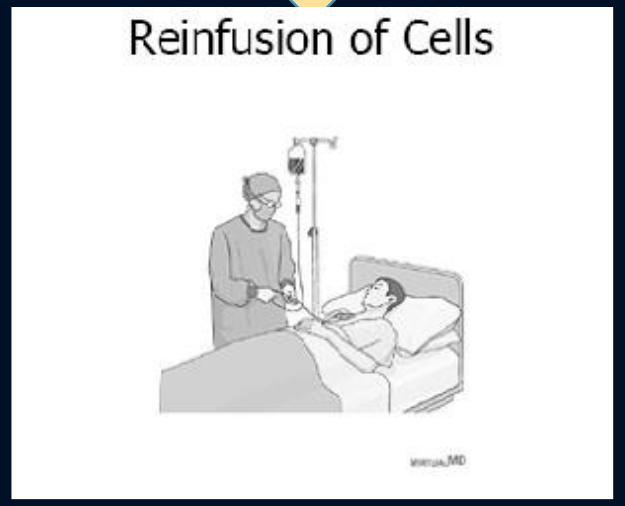


Chronic Rejection

HLA Antibodies. From association to causation of chronic graft failure. 2008. Terasaki

Presence of HLA antibodies is the cause of Graft rejection in solid organ transplantation

Debates in Stem cell transplant



HLA Antibodies

Being sensitized is not the obstacle

22-25%

Is there any relevant anti HLA antibody in highly sensitized patient

DSA ?

Donor Specific Anti-HLA Antibody and Risk of Graft Failure in Haploidentical Stem Cell Transplantation

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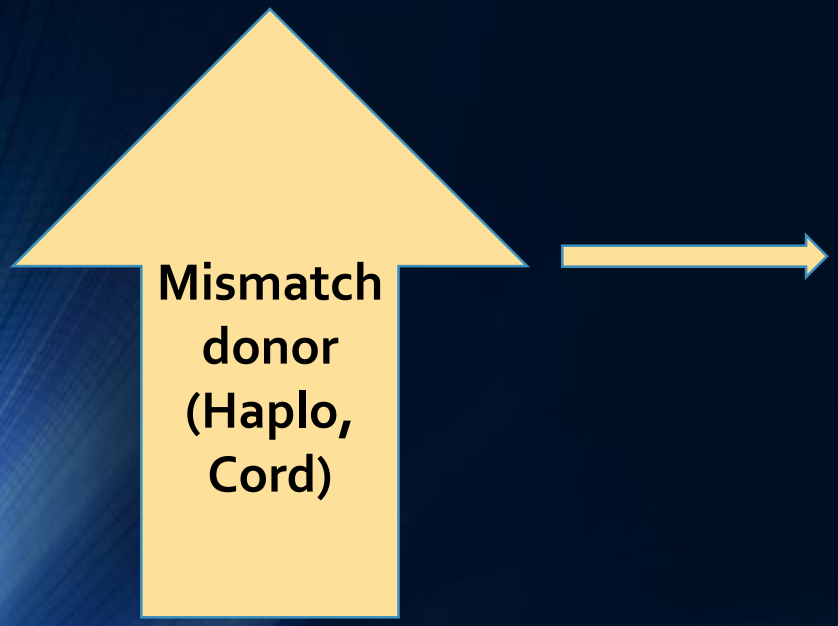
The rates of graft failure presence in 57% in patients who had DSAs

DSA in Haplo-identical SCT

The reported prevalence of anti HLA-Antibodies is approximately 20-25% in patients undergoing Haplo-identical SCT.



Facilitate detection of DSA as a major cause of graft rejection in stem cell transplantation

24% of Haplo-identical recipient has DSA

Piyanuch, Advances in Hematology.V 2016

DSA and Haplo-identical SCT

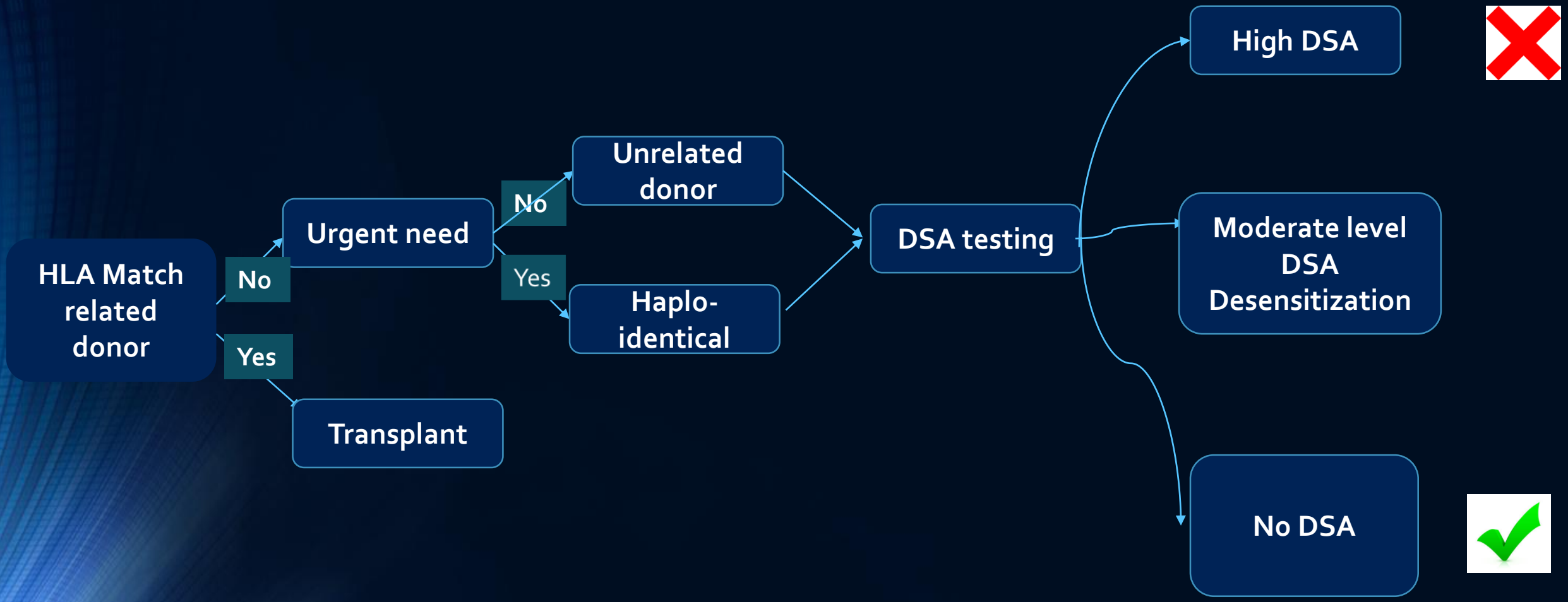
- 79 patients receiving Haplo-SCT
  - 16 (20%) were sensitized with HLA antibodies
  - 9 (56%) has DSA
  - The engraftment of patient with DSA was 61% versus 94% with absence of DSA.

Yoshihara et al. Bone Marrow transplantation, vol.47,no,4,pp 508-515 2012

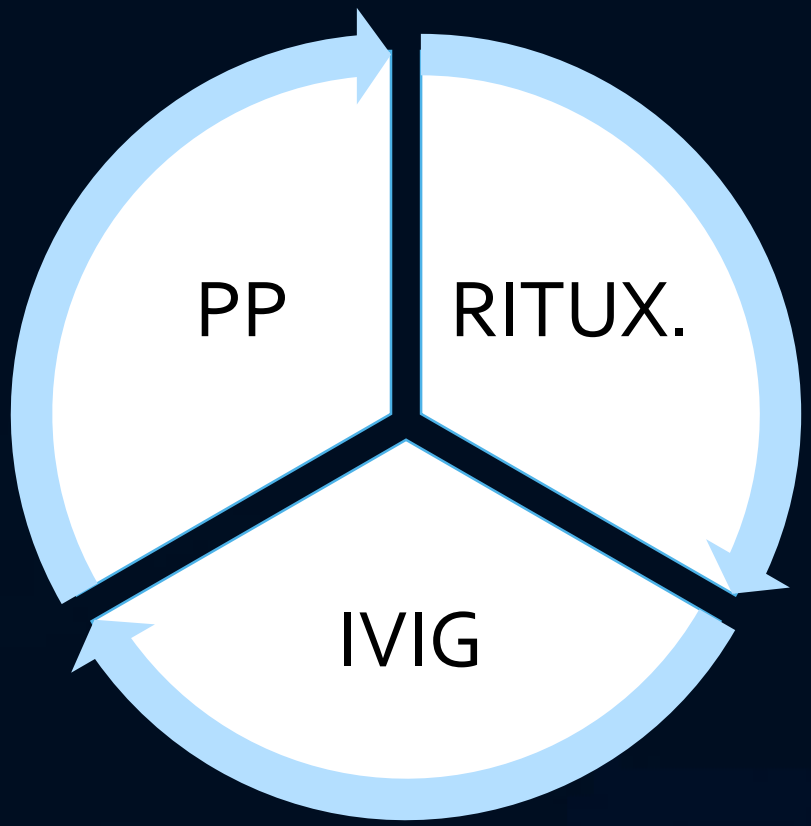
Prevalence of DSA

- Recipient gender : (86% Female) (5% Male)
- More often in "Child to Mother" Haplo- identitical SCT.

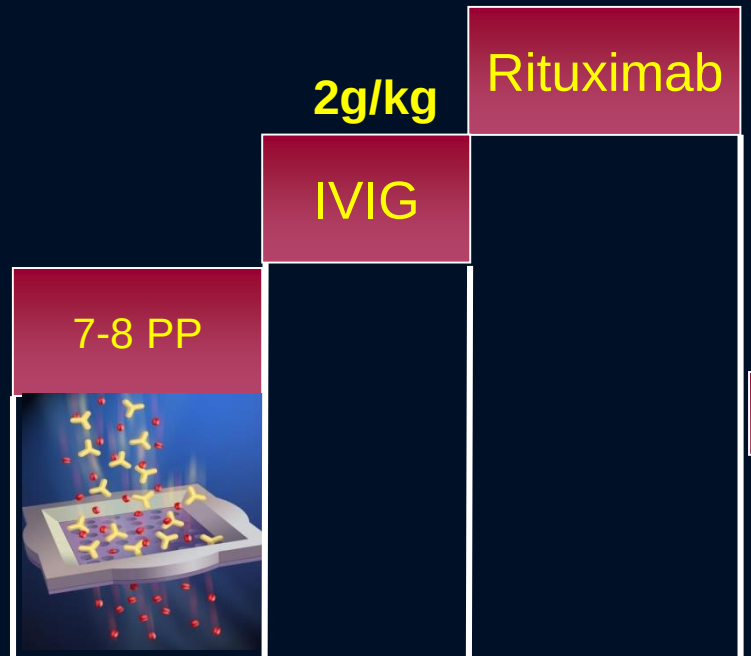
SCT scheme at KFSHRC



Desensitization protocol " DSA removal"



Pre Transplant



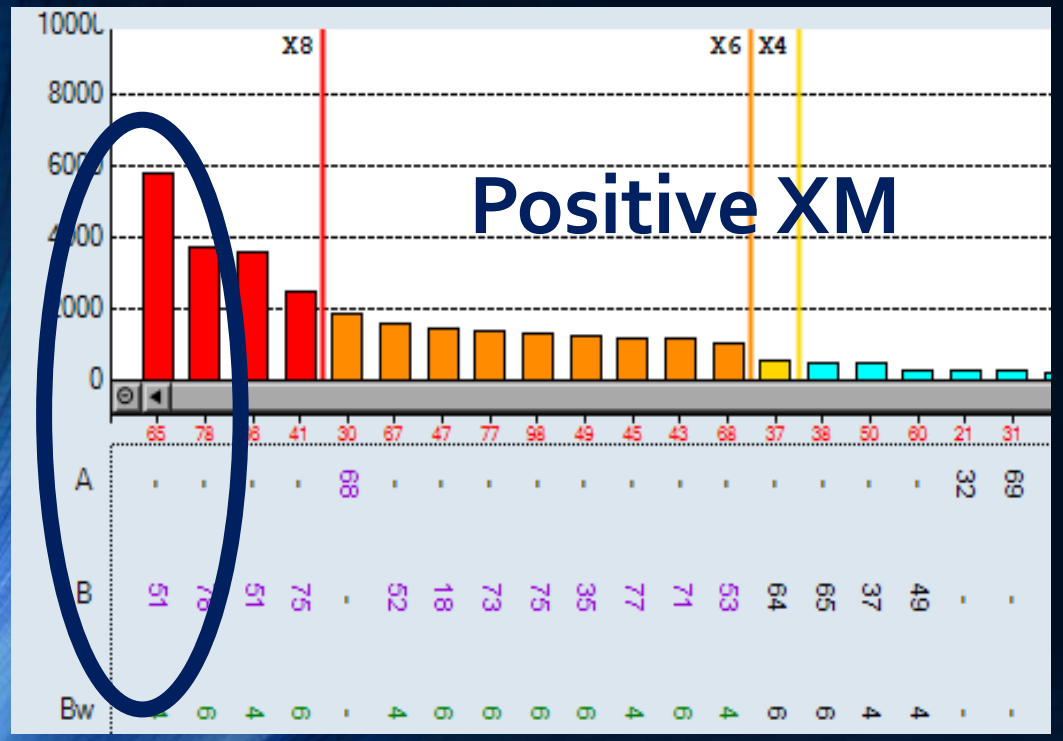
Weekly HLA antibody assessment

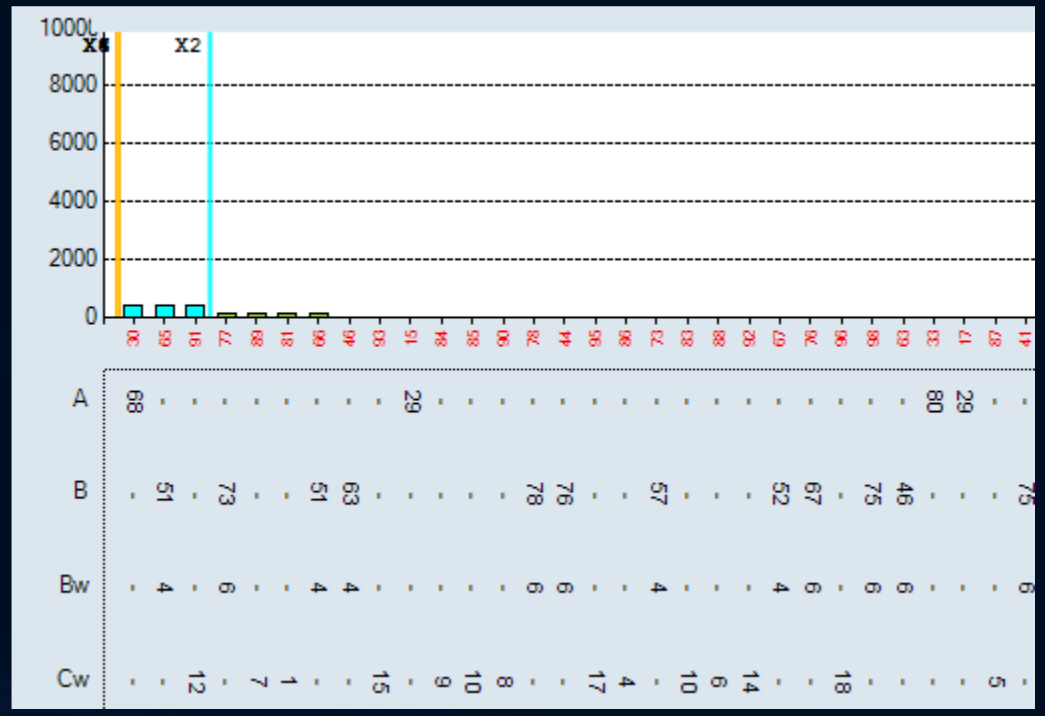
Haplo identical transplant at KFSHRC

- 52 Haplo-identical SCT performed
- 14 (27%) patients were sensitized to HLA antigens
- 4 (29%) patients demonstrate DSA
  - 1 Death
  - 3 less than 1 year with excellent engraftment.

Haplo-Identical SCT with DSA

	A	B	C	DR	DQ
Recipient (Mother)	A*33	B*44 B*50	C*02 C*06	DRB1*01:02 DRB1*13:01	DQB1*05:01 DQB1*06:03
Donor (Son)	**A*31** A*33	B*50 **B*51**	C*02 **C*07**	DRB1*13:01 **DRB1*15:01**	**DQB1*06:02** DQB1*06:03





Flow cytometry Crossmatch for CD34

OR30. HLA expression on CD34+ stem cells: is a flow cytometric crossmatch a good gatekeeper for mismatched hematopoietic cell transplantion?

Maria P. Bettinotti [1], Donna P. Lucas [1], Gabriel Ghiaur [2], Annette M. Jackson [2], Douglas E. Gladstone [2]

Figure 1 - HLA surface expression: average of 10-13 different donors

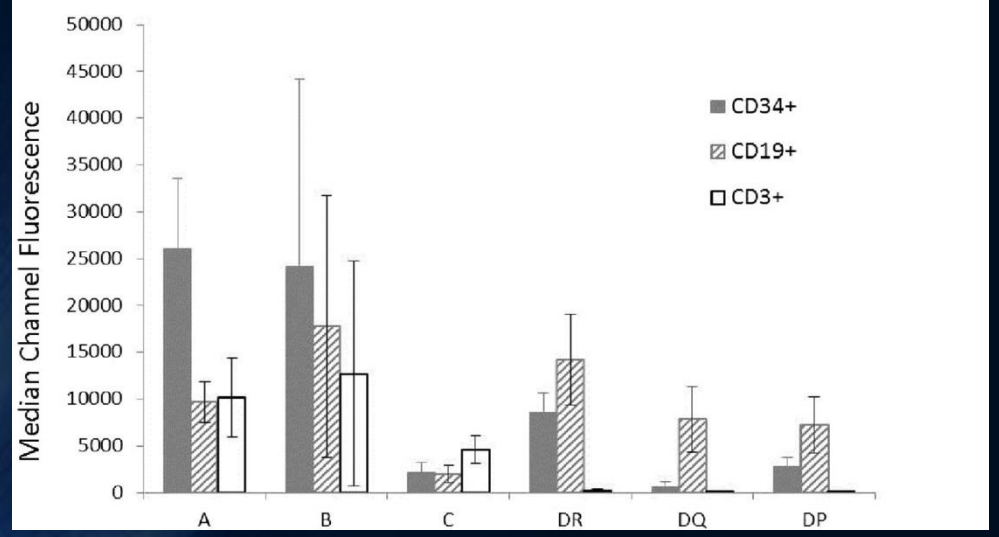
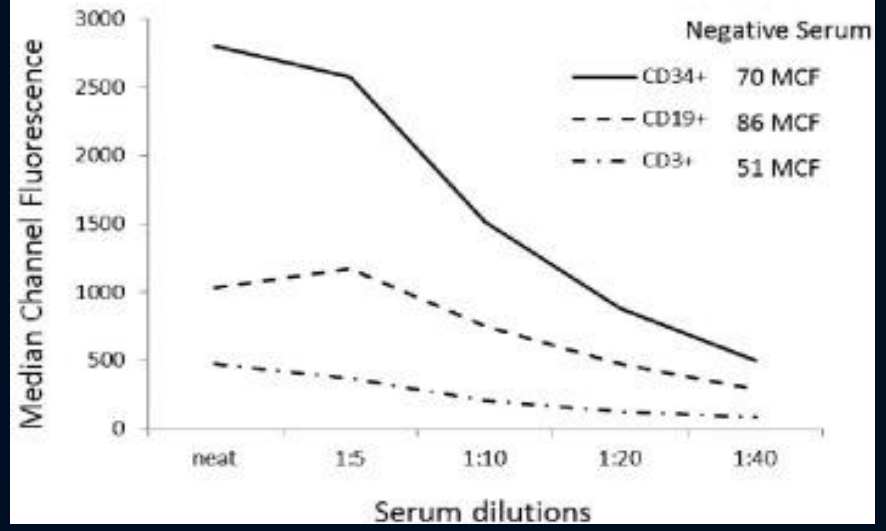


Figure 2 - BM sample + serum with HLA-A2 DSA



humimm.2018.07.035

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Conclusions

Antibodies specific for all class I and II HLA targets may be deleterious given their expression on CD34 + cells. HLA-A and B specific antibodies may be especially harmful given the high expression of these loci. Use of peripheral T and B donor lymphocytes flow cytometric crossmatch may underestimate the risk of graft failure due to the relative lower expression of HLA-A and B loci in these cell populations.

Conclusion

Globally , in the past 5 years much has been learned about the risk of DSA in Haplo-Identical transplant.

DSA impact on the development of graft failure

Donor selection with carful HLA antibody assessment shall be considered.

Several successful studies on treatment for allo-sensitized patients and now can be more safely undergo a transplant with Pre existing DSA