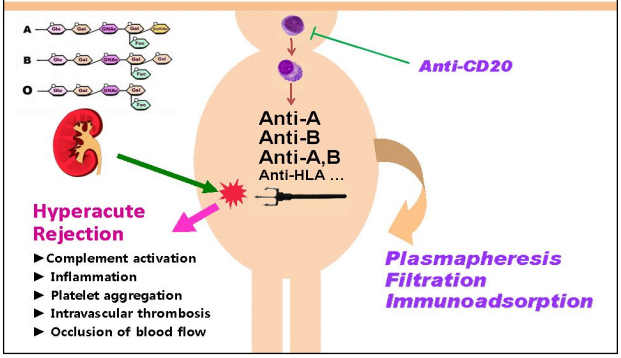
Mini-Lecture 2

Isoagglutinin Titer in ABO-i KT A Practical Approach

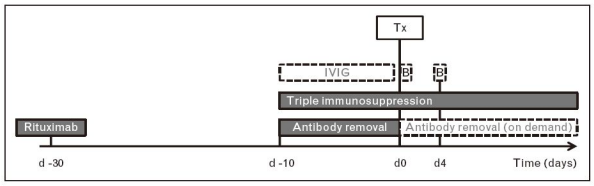
Seog-Woon Kwon, MD

Department of Laboratory Medicine Asan Medical Center, Seoul, Korea

Preformed Antibodies



Standard desensitization protocol



Curr Opin Organ Transplant 2012, 17:376-385

Issues to be considered

- Pre-KT target titer: ≤ 4 ?
- Post-KT titer maintenance: < 16 ?
- Post-KT Ab removal criteria: ≥ 16 ?

The lower, the better ?

IgM vs. IgG ?

Titration methods ?

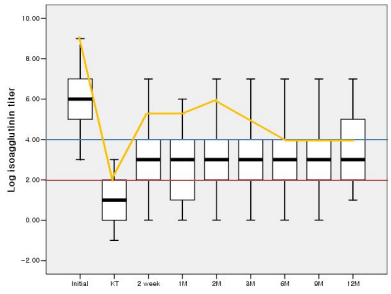
Institutional variation ?

IgM vs. IgG

	Distribution	Reactive Temperature	Complement activation	Binds to FcR on phagocytes
IgM	Intravascular	Cold > Warm	highest	low affinity
IgG1	Mainly extravascular	Warm > Cold	second-highest	high affinity
IgG2			third-highest	extremely low affinity
IgG3			highest	high affinity
IgG4			no	intermediate affinity

Group A & B : Anti-A & Anti-B (Mainly IgM)
Group O: Anti-A, Anti-B & Anti-A,B (Mainly IgG)

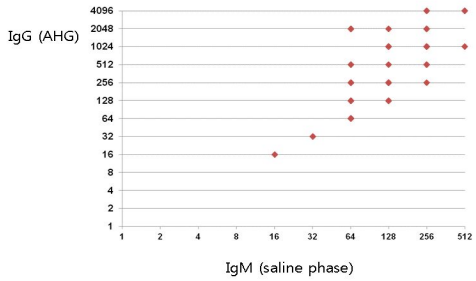
Changes of Isoagglutinin titers (IgM)



N=95

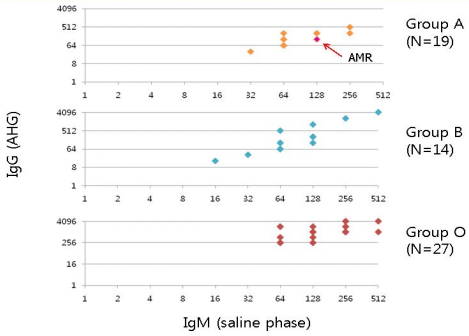
AMR: 1 case
B(D)→ O(R)
Initial titer: 512
Pre-KT PP: 12
Titer at KT: 4
Titer at AMR: 32
Post-KT PP: 4
Cr at AMR: 1.2
Recovered by steroid pulse

Correlation of IgM & IgG

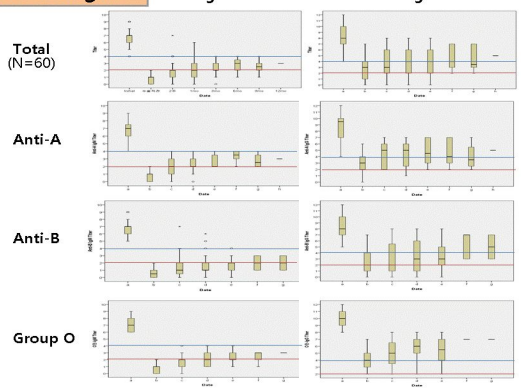


N=60

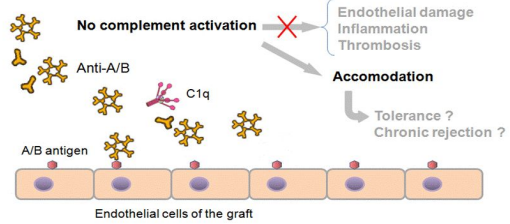
Correlation of IgM & IgG according to blood group



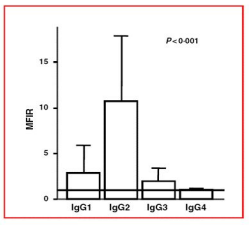
Titer changes



Accommodation



Anti-A/B IgG in group O donors



N=15

Fig 3. Anti-A/B IgG subclass analysis in sera of 15 blood group O donors: IgG subclasses were analysed by ABO-FACS in 15 blood group O donors with high anti-A/B IgG levels. The bars represent mean values (+SD). All six 15 donors were positive for the IgG2 subclass, whereas seven donors were positive for IgG1 and four donors for IgG3. IgG4 was negative in all samples. The differences among the four subclasses were statistically significant using a Kruskal–Wallis test as indicated by the *P*-value. The detection limit (MFIR = 1) is indicated with a horizontal line.

Br J Haematol 2005;130:954–963

Anti-A/B response posttransplantation

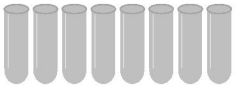
IgM+IgG+IgA
IgM+IgA
IgM+IgG
IgG1+G2
IgG2 only
IgM+IgA2
IgM+IgG1
IgM+IgG1+G2+G3

← Cytokines in microenvironment

Isoagglutinin titration: Methods

- Tube test
- Micro Typing System
- Column Agglutination Technique (CAT)
- Flow cytometry

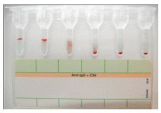
Isoagglutinin titration: Tube Test



Serial dilution

Saline phase: RT
AHG (Anti-IgG/C3d): 37°C
DTT or 2ME: destroy IgM
End point: 1+ or ± ?

Isoagglutinin titration: CAT

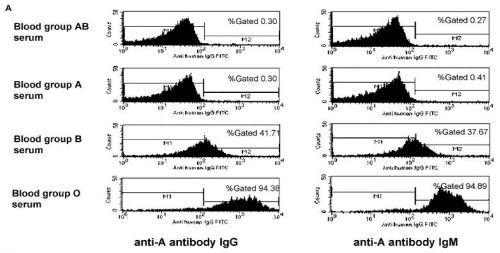


Serial dilution

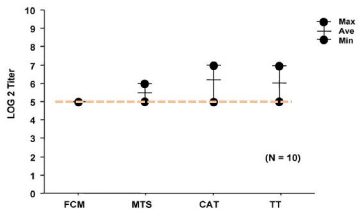
Saline phase: RT
AHG (Anti-IgG+C3d): 37°C
DTT or 2ME: destroy IgM
End point: 1+ or ± ?

Isoagglutinin titration: Flow cytometry



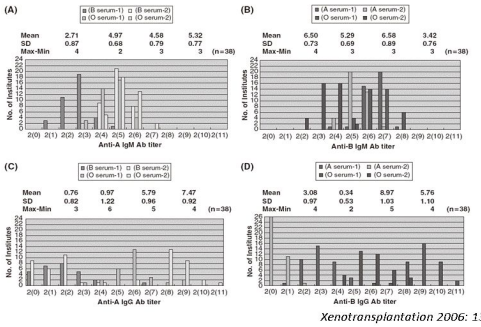


Reproducibility of assay techniques



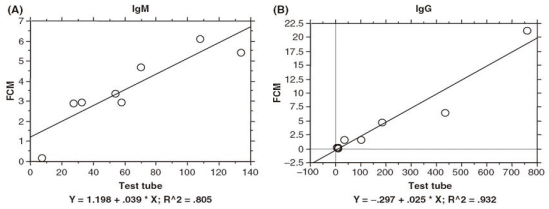
Tanabe K. Transplantation 2007;84: S13-S16

Institutional Variation (Tube Test)



Xenotransplantation 2006: 13: 136–140

Correlation btw mean values measured by tube test and flow cytometry



Xenotransplantation 2006: 13: 136–140

Summary

Further studies are needed to establish:

- Pre-KT target titer (IgM vs IgG ? High titer exclusion ?)
- Post-KT Ab removal criteria (IgM vs IgG ?)
- Standardization of titration methods
- Mechanism of accommodation