ABO i

Kidney Transplant

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ABO Compatibility Chart

If you have blood type...	You can normally receive a kidney from a donor with the blood type:	You can normally donate a kidney from a donor with the blood type:
O	O	O, A, B, AB
A	A, O	A, AB
B	B, O	B, AB
AB	O, A, B, AB	AB

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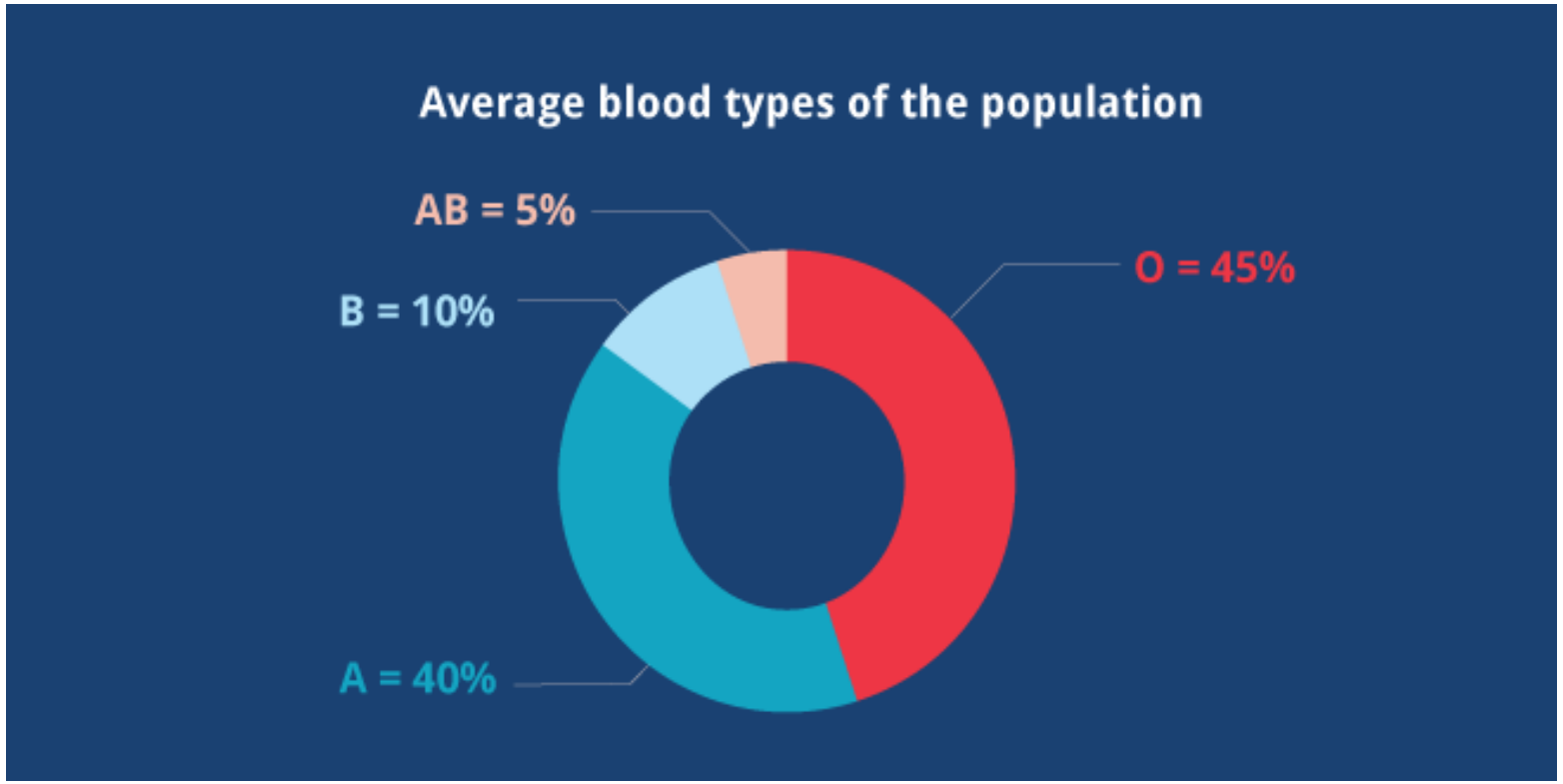
Blood Type US Population



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ABO Antibody Characteristics

- Appear after birth, peaking at 5-10 years of age
- Predominantly IgM
    - Group O individuals form IgG
- Complement binding at 37 ℃
- Titers range from 4 ≥ 2048

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Clinical Significance

- **Hemolytic transfusion reaction**

  Recipient ABO antibody reacts with donor RBC and activates C', resulting in the destruction of transfused RBCs.

- **Hyperacute rejection**

  Recipient ABO antibodies react with donor ABO antigens. C' is activated at the surface of endothelial cells, resulting in rapid destruction of the cells.

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History of ABOi Renal Transplant

- Living donors non A2 with intensive pre-transplant conditioning of recipients
- Survival rates lower than ABOc, but promising results
- 20 years later – widespread adoption in Europe
  - 2005-2012: 1420 Living Donor ABOi
  - Varying desensitization and IS protocols
  - Overall graft survival at 3 years comparable to ABOc

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Japanese Experience

- No deceased donors
- 1 year graft survival 96%, 5 year 91%
- 30% of living donor transplants are ABOi
- > 1400 transplants to date

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ABO Antigen Incidence by Population

Incidence (%)				
Phenotype	Caucasian	African-American	Asian	Genotypes
A_1	34	19	27	A_1A_1, A_1A_2, A_1O
A_2	10	8	Rare	A_2A_2, A_2O
B	9	19	25	BB, BO
A_1B	3	3	5	A_1B
A_2B	1	1	Rare	A_2B
O	44	49	43	OO

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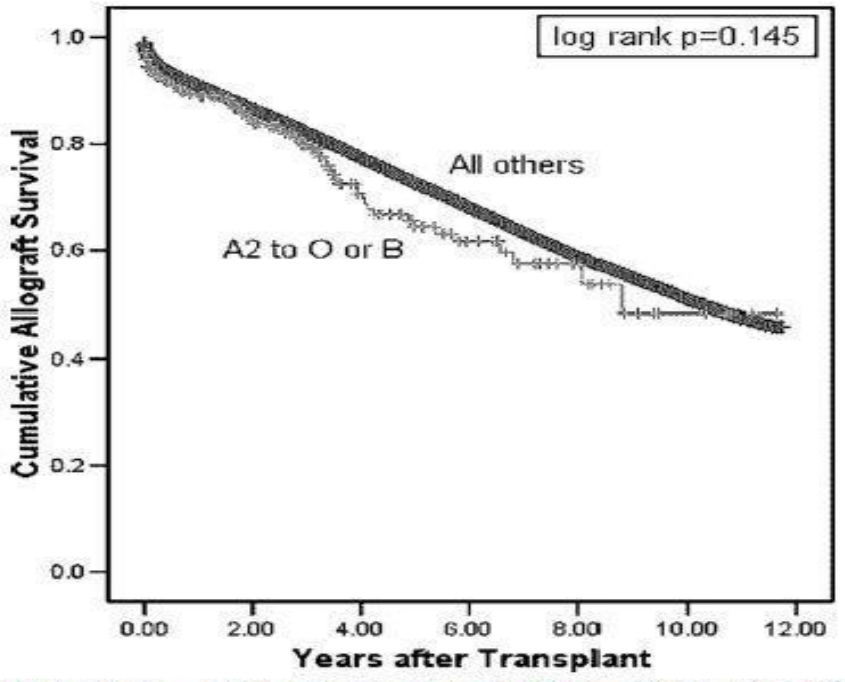
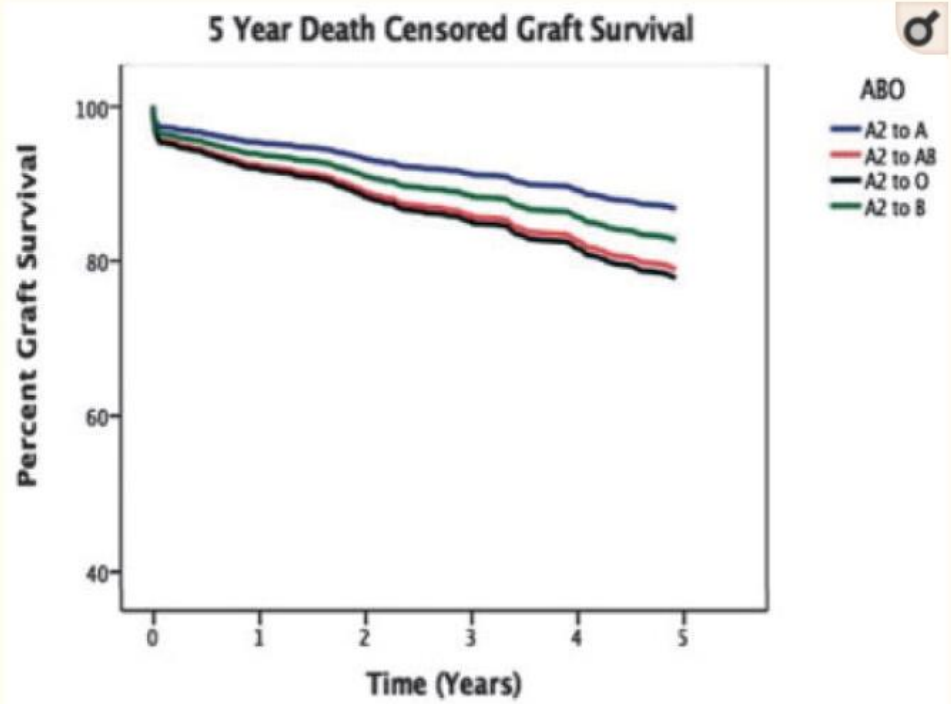
Graft Survival

Graft Survival: Non-A1 to B or O





5 Year Death Censored Graft Survival

ABO	P Value	Hazard Ratio	95.0% CI	
			Lower	Upper
A2 to A (Reference)				
A2 to AB	0.115	1.668	0.883	3.151
A2 to O	0.094	1.768	0.907	3.448
A2 to B	0.294	1.343	0.774	2.332

Fig. 1

Five year death censored graft survival estimated by Cox regression analysis.

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Clin Transplant, May 2012

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KAS Update for Group B Candidates

Blood Types A, non-A_1 and AB, non A_1B

Kidneys may be transplanted into candidates with blood type B who meet *all* of the following criteria:

1. The transplant program obtains written informed consent from each blood type B candidate regarding their willingness to accept a blood type A, non-A_1 or blood type AB, non-A_1B blood type kidney
2. The transplant program establishes a written policy regarding its program's titer threshold for transplanting blood type A, non-A_1 and blood type AB, non-A_1B kidneys into candidates with blood type B. The transplant program must confirm the candidate's eligibility every 90 days (+/- 20 days).

A2 or A2B deceased donors to B recipients at MCD

Anti-A1 IgG at room temp < 1:8

Repeat every 90 days

No desensitization

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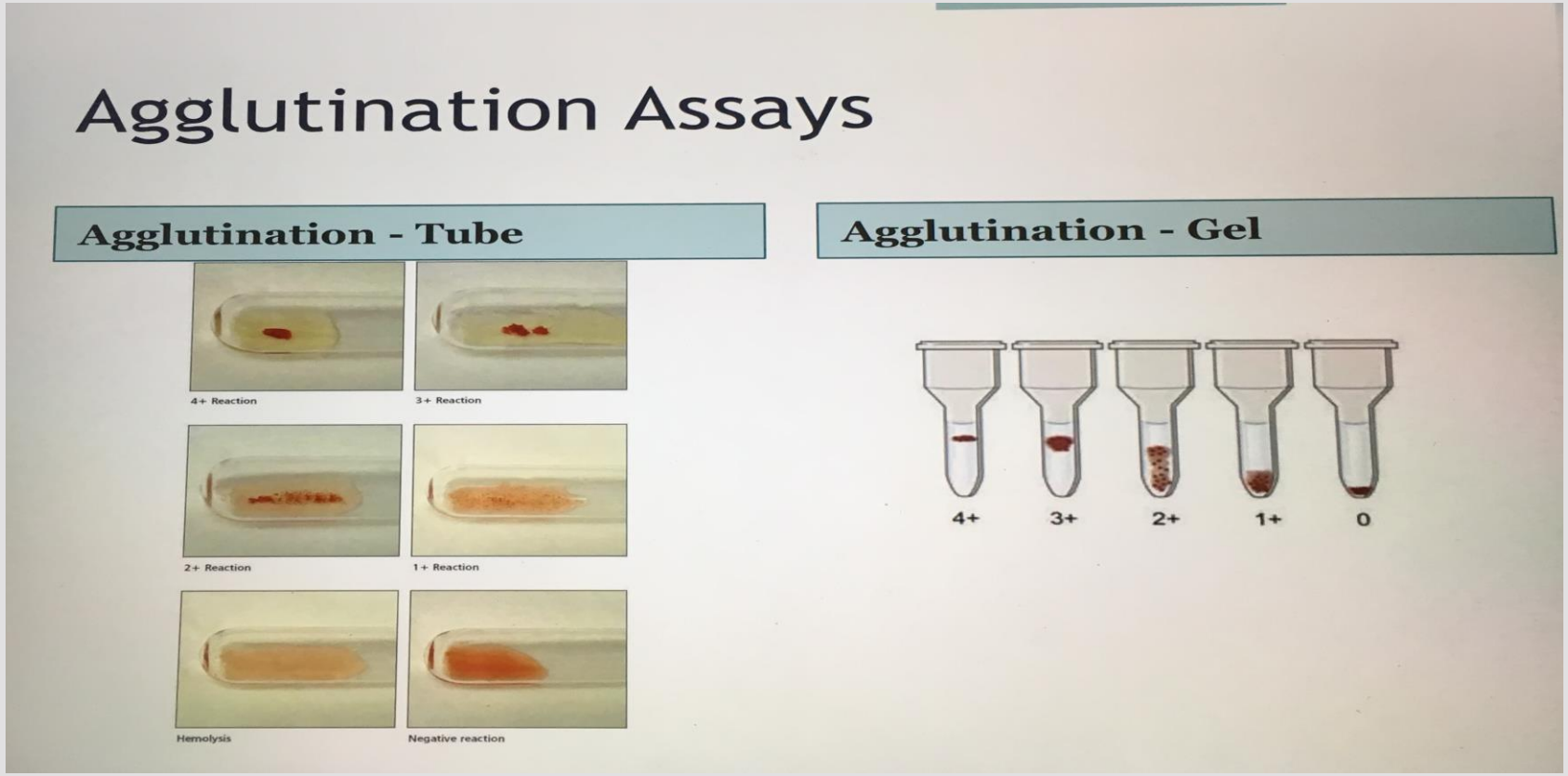
Agglutination Assays



ABO I Live Donor

- All ABOi pairs are entered into KPD
- Baseline anti-ABO titer IgG at IAT
- Insurance must agree to pay for desensitization
- Careful informed consent from donor and recipient
- Begin desensitization protocol

Desensitization

- Begin immunosuppression
- PP/IVIG daily until anti-ABO titer <1:8 IgG IAT
- Retuximab day -1
- Thymoglobulin 5mg/kg, Mychophenolate, Steroids post
- Measure anti-ABO titer daily X 2 weeks post, then every 2-3 days x 1 week

Desensitization

- PP/IVIG post if anti-ABO titer >16
- Kidney biopsy if creatinine does not fall or for any acute elevation
- PP/IVIG for AMR
- Complement inhibitors, proteaosome inhibitors for resisistant AMR
- Increase incidence AMR 0-28 days post
- 3-year graft survival same as ABOc

IgM Titers

Data is limited

A few studies – IgM > 32 early acute rejection/thrombotic microangiopathy

Other studies-IgM not associated with rejection or outcome

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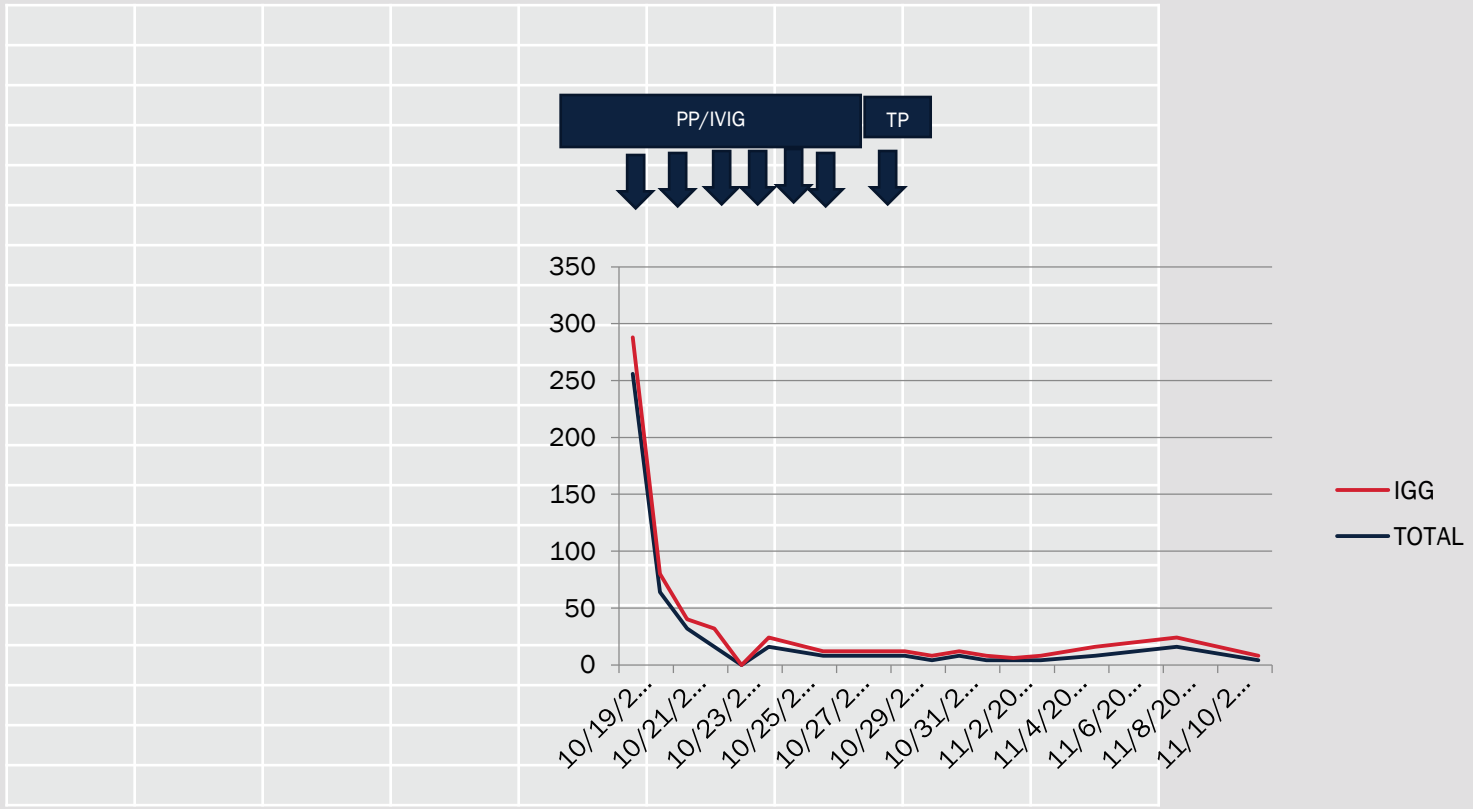
Summary

- Long-term graft outcome of ABOi is comparable to ABOc
- Each center must develop their own protocol to qualify group B patients to receive non-$A_{1,}$, non- A1,B DD kidneys
  - Acceptable anti-A titer for inclusion in program based on titration methodology
  - Consent form for receipt of ABOi organ
  - Pre-and post- transplant monitoring and treatment plan
- Close communication required with blood bank/transfusion service to develop testing protocol
  - Pre-transplant considerations: methodology, frequency of testing, sample age and type, turn-around time
  - Post-transplant consideration: routine monitoring vs treatment of rejection, use of PP/IVIG

Live B donor to O recipient



Questions