

TRANSPLANT

Donation

Donor requirements

No malignancies, uncontrolled infections, HIV, most chronic medical problems

Brain death criteria:

- No spontaneous respirations
- Unresponsive to stimuli
- No pupillary, corneal, oculocephalic reflexes
- Apnea test or EEG
- Pt must be normothermic and on no sedating meds

Extended kidney donation criteria: >60, Cr >1.5, HTN

Hypothermic continuous pulsatile machine perfusion w/ colloid: 96hr renal preservation time

ABO match done for all transplants

Crossmatch determines presence of pre formed Abs in recipient (Ab to HLA)

Panel reactive antibodies: test for Abs to known HLA types

Chromosome 6p contains loci for humoral and cellular immune responses

Class I Ag: (HLA A,B,C) on all nucleated cells; autosomal codominant inheritance

Class II Ag: (HLA D, Dr, Dq, Dp) on antigen presenting cells

Mixed lymphocyte cx (MLC): defines cellular arm of imm response

Dr-matched renal transplants have 20% higher success rate

Ab production: Mφphg ingests Ag, present to Th cells and secrete IL 1; Th cells secrete IL 2 and increase Th cell production; Th cells stimulate B cell production via IL 4; B cells differentiate into plasma cells and secrete Abs

Rejection

-Hyperacute: mins to hours post op; d/t preformed Ab (usu ABO or HLA); irreversible; rare
Accelerated acute- POD 7-10; d/t Abs or T cells

-Acute: days to weeks; d/t T cells; 20-30% of cadaver donor transplants; good Px w/ increased immunosuppression dose

-Chronic: years; d/t immune and non immune causes; poorly understood; no good Rx

Immunosuppression

Maintenance Rx vs rejection Rx

Immunosuppressives always used in combo

10-100x increase in risk of lymphoma and skin cancers

1. Steroids

Lympholytic & inhibit IL 1

Maintenance & rejection (higher doses)

2. Cyclosporine

Inhibits secretion of IL 2 (T cell growth factor)

Maintenance only

Cx: nephrotoxic (dose dep), hepatotoxic, HTN, hyperK/uricemia/lipidemia

Clonidine or CCB used to treat HTN

P450 metabolized

3. Tacrolimus (prograf, FK-506)
 - Inhibits IL 2 production
 - More potent than cyclosporine: inhibits B and T cells
 - Maintenance & rejection
 - Cx: nephrotoxic, neurotoxic, hyperglycemia
 - P450 metabolized
4. Mycophenolate mofetil (cellcept)
 - Inhibits IMP (inosine monophos) Dehydrogenase (specific to T & B cells)
 - Maintenance
 - Cx: GI intolerance (diarrhea)
5. Sirolimus (Rapamycin)
 - Antifungal macrolid inhibits IL 2 pathway; binds TOR
 - Used as an adjuvant to steroids or calcineurin inhibitors
 - Cx: impaired wound healing, dyslipidemia
6. Thymoglobulin (antithymocyte) and ATGAM (antilymphocyte)
 - Polyclonal sera; used only for induction or acute rejection
7. OKT3
 - Monoclonal Ab to CD3 receptor
 - Induction or acute rejection only
8. Daclizumab (Zenapax), Basiliximab (Simulect)
 - Monoclonal Ab to IL 2 receptor
 - Induction

Renal transplant

Pt's on dialysis for 2 years have 3x higher risk of graft failure than pts on dialysis for < 6 mos

Mortality on dialysis: 1yr: 22%; 5 yr 60%

Renal transplant pts live an average of 10 years longer w/ transplant

Renal vessels attached to iliac vessels; ureter into bladder

Left kidney preferred d/t long L renal vein

NL fxn returns in 3-5 days for LRD and 7-15 days for cadaveric

S/Sx of acute rejection:

1. Fever
2. HTN
3. Low UOP
4. Proteinuria
5. Increasing Cr (DDx: dehydra'n, ATN, obstruc'n, lymphocele, infxn)

CMV is most common infection (peak at 4-6 weeks post op)

P/w fever, malaise, weakness, GI bleed, esophagitis, ophthalmitis, cerebritis

Rx: acyclovir

SURVIVAL %	1 year	5 year	10 year
Cadaver: graft	88	63	37
Cadaver: pt	94	80	60
Living: graft	95	76	55
Living: pt	97	90	80

Liver transplant

#1 indication in US: cirrhosis secondary to Hep C

Prioritized according to MELD score (Bilirubin, INR, Cr)

ABO matched only

Require size match unless lobe transplant

Adults: R lobe transplant

Kids: L lobe transplant

Acute rejection less common and milder than with renal transplant

Px: 85% 1 yr pt and graft survival if transplanted before terminal phase