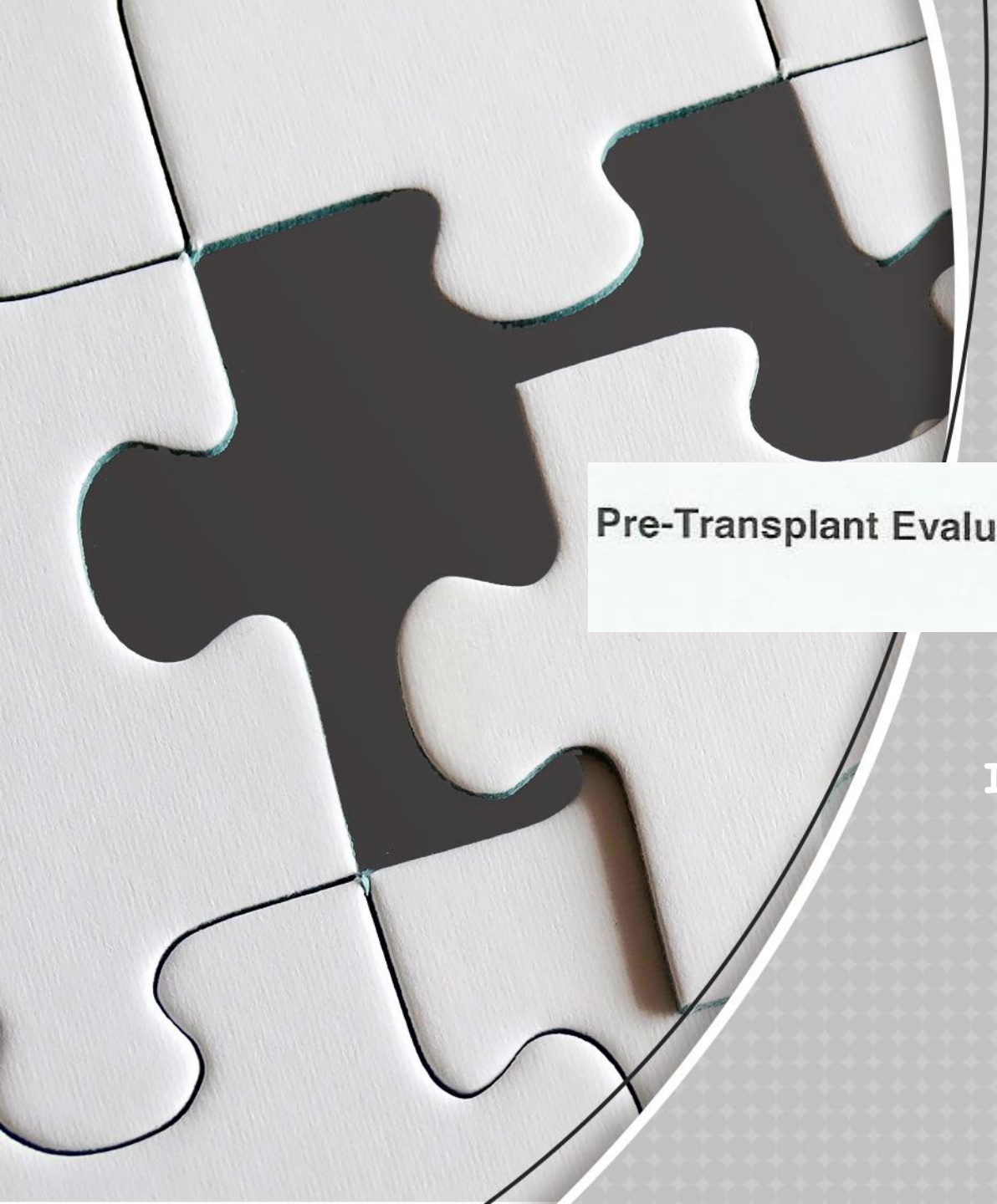

Pre-Transplant Evaluation of Recipients / Donors

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athens-NEPHROLOGY

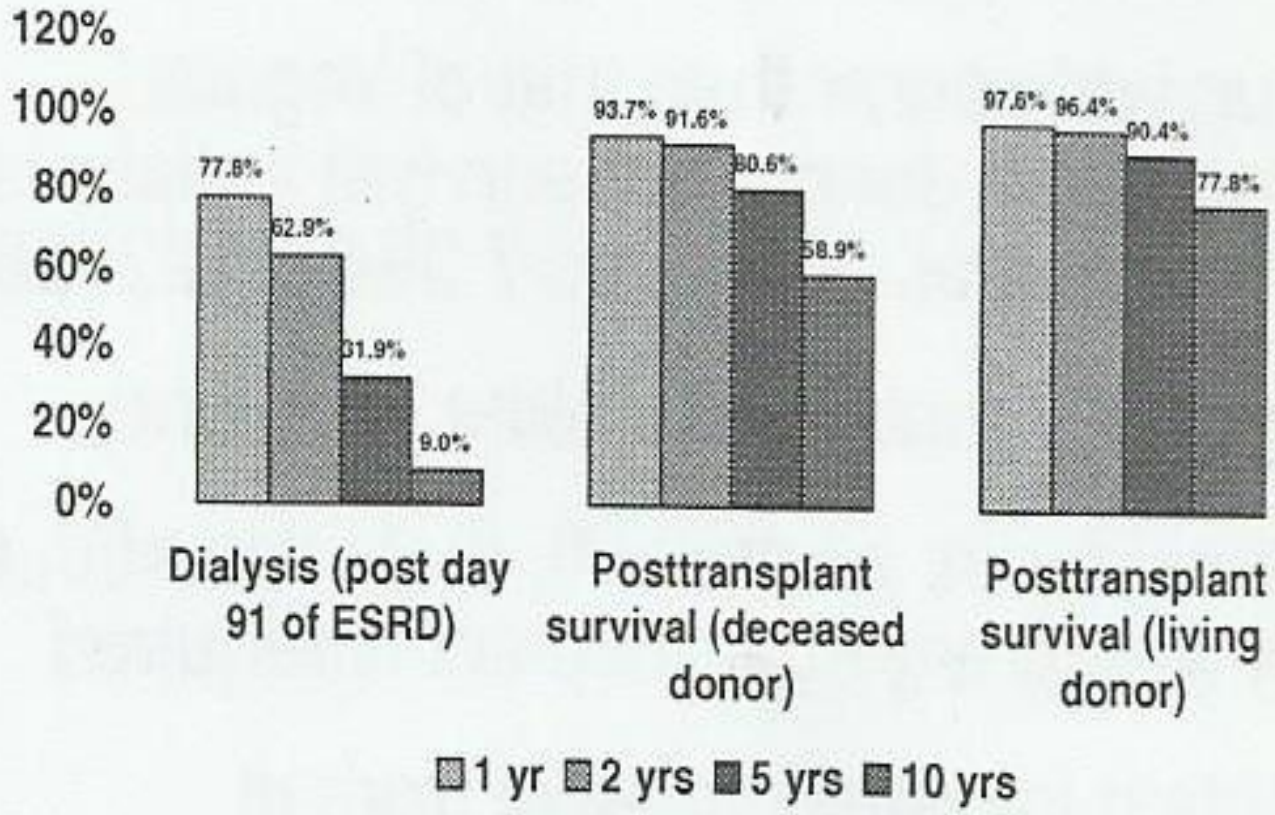
Purpose of the Evaluation - Summary

- Assess patient's medical, surgical and psychological suitability for transplant
- Understand the patient's reasons for wanting a transplant
- Discuss risks vs benefits of transplant
- Discuss donor options
- Plan the immunosuppressive protocol ahead of time

The Big Questions

- Will this pt benefit from transplant (survival, quality of life)? Wolfe et al. NEJM 1999;341: 1725
- Is it appropriate to ask a living donor to donate?
- Is it appropriate to 'take' a deceased donor kidney from the list? (Responsibilities to individual pt and to the list)

ESRD Survival by Treatment Modality



National Kidney Foundation. Available at: http://www.kidney.org.

Discussion with Patient - I

- What is the pt's understanding of risks and benefits of transplantation?
- Is pt aware transplant is not a zero-risk procedure?
- Is pt aware of the types of transplants and of live donor exchanges?

Discussion with Patient - II

- Is pt suitable for / interested in *expanded criteria* donors?
- Is pt suitable for / interested in HCV Ab+ positive donors?
- Is pt suitable for / interested in HBV cAb+ donors?

Expanded Criteria Donors

- Another source of allografts
- Survival poorer than that of 'regular' deceased donors but survival > dialysis Merion et al. 2005 Dec 7;294 (21):2726-33
- Typically matched to older recipients
- Consider in: all pts >60, diabetics >50, any pt where urgent transplant is required
- Obtain informed consent from pt

Advantages and Disadvantages of Living-Donor Transplantation

Advantages	Disadvantages
• Preemptive transplant option • Can select donor for haplotype match, age • Better outcomes • Minimal delayed graft function • No wait for deceased-donor kidney • Can time transplant for convenience • Immunosuppressive regimen may be less aggressive • Emotional gain to donor	• Psychological stress to donor • Long donor evaluation process • Operative donor mortality (~1/3000 patients) • Major complications (0.2%-2%) • Minor complications (~50%) • Potential donor hypertension, proteinuria • Risk of trauma to remaining kidney • Risk of unrecognized covert renal disease

Kendrick E, et al. In: Danovitch GM, ed. *Handbook of Kidney Transplantation.* 2005:135-168.

Living Donor Evaluation

- Donor's risk must be considered separately from recipient's need for transplant
- Donor must be informed of the risks
- ABO blood-type compatibility, tissue type, and crossmatch are initial screening steps
- With multiple suitable donors, the transplant center will help determine the best donor
  - For a younger recipient who may require a second transplant, a parent may be selected over a sibling, whose kidney may be needed in the future

Living Donor Evaluation (cont'd)

Medical history and physical exam
Comprehensive lab screening
- Blood count/chemistry panel
- HBV, HCV, HIV, and CMV tests
- Glucose tolerance test

Urinalysis
- 24-hour protein and creatinine

Cardiovascular workup
- Chest X-ray
- ECG
- Exercise treadmill for donors older than age 50

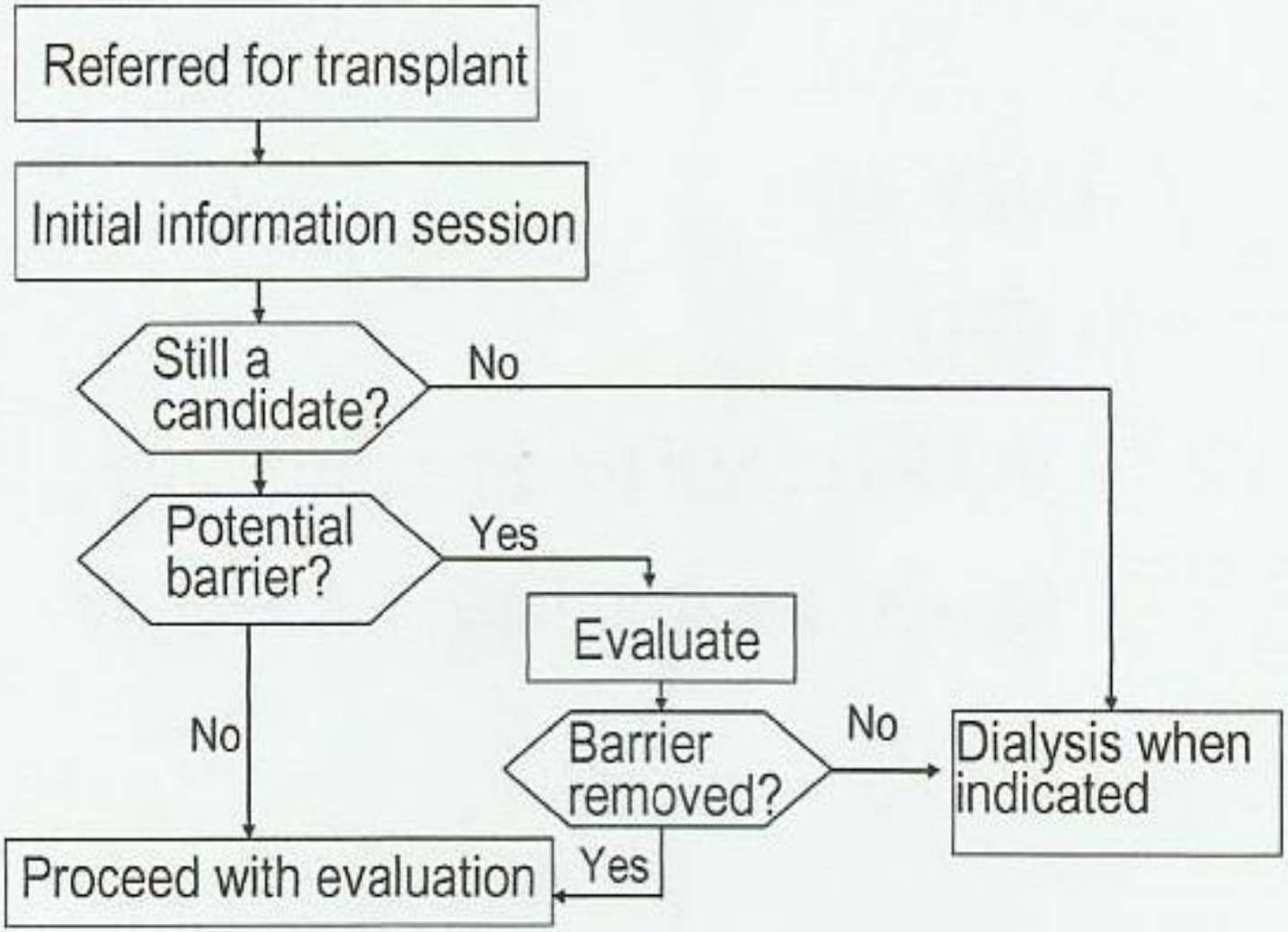
Helical CT urogram
Psychosocial evaluation
Repeat crossmatch before transplant

Contraindications to Kidney Donation

- Age
  - <18 years or >65-70 years
- Hypertension
  - >140/90 mm Hg or need for medication
- Diabetes
- Proteinuria
  - >250 mg/24 hours
- GFR <80 mL/min
- Microscopic hematuria
- Multiple renal vessels
- Significant medical illness
- History of thrombosis or thromboembolism
- Strong family history of renal disease, diabetes, or hypertension
- Psychiatric conditions or substance abuse
- Pregnancy

Kasiske BL, et al. *J Am Soc Nephrol.* 1996;7:2288-2313.

Kidney Transplant Evaluation Process



Adapted with permission from Kasiske BL, et al. *Am J Transplant.* 2001;1 (suppl 2):1-95.

History - I

- Cause of ESRD
- Previous transplants
- Previous pregnancies, RBC transfusions
- CV disease (exercise tolerance, evidence of PVD)
- Cancers
- Other diseases
- Previous immunosuppression (previous transplant, SLE etc)

History - II

- Compliance
- Social supports
- Family Hx (of renal disease, DM)
- Functional status
- Urine output; problems with urination (males)
- Possible living donors

Examination

- General exam
- BMI
- Exclude overt CV disease and overt neoplasia
- Femoral pulses – volume, bruits
- Feet in diabetics
- If the pt is frail - assess their walking

Routine Tests

- ABO, HLA typing, Panel Reactive Antigen (PRA)
- EKG, CXR +/- cardiac stress tests +/- TTE
- HBV sAg, HBV sAb, HCV Ab, CMV Ab, HIV Ab, syphilis
- Pap smear in all women; mammogram >40yrs
- Stool guaic or colonoscopy if >50yrs

Immunizations in Adults

- Before transplant (at least 4 wks; longer if live attenuated)
- Viral: HAV, HBV*, influenza*, VZV
- Bacterial: pneumococcus

*May need yearly booster

Stark et al., Lancet 2002; 359: 957

Contraindications to Transplant

- Active cancer
- Active infection (acute or chronic)
- Active psychiatric illness
- Ongoing non-compliance / substance abuse
- Major morbidity which would be worsened by transplant or lead to very short post-transplant survival
- Severe obesity

Cancer

- Risks of faster tumor growth and 'wasted' kidney
- Minimum 2 yrs disease free; some minimum 5yrs (melanoma, breast)
- Oncology input
- Std screening for breast, colorectal, prostate, uterine cervix cancers

Chronic Infection

- Diabetic foot ulcers
- Osteomyelitis
- HIV – not a C/I if controlled; refer to special center
- HCV related advanced cirrhosis (? list for liver plus kidney)

Psychiatric Illness

- Often treatable and not a C/I
- Ongoing substance abuse a C/I
- Mania: minimize steroids; avoid lithium if possible (? valproic acid)

Non-Compliance

- Common-sense assessment
- Compliance to dialysis regimen, meds
- Talk to local nephrologist and dialysis unit
- Formal psychiatric assessment in some cases
- Many pts improve with time (on dialysis)

Obesity

- Increasingly common
- Most pts gain weight after transplant
- ↑ risk of early complications: wound infection, wound dehiscence
- ↑ risk of later complications: DM, possibly poorer allograft survivial
- Most evidence suggests transplant still better than dialysis
- Evidence that BMI >41 is not a/w survival benefit compared to dialysis

Obesity – Practical Approach

- Ideally BMI < 30 but difficult to achieve
- In general, aim for BMI <35
- Judge each case on an individual basis e.g. the young obese pt with no CAD may do very well with a transplant
- Consider steroid – free protocols

CV Disease: Background

- Important to distinguish *peri-operative* and *long-term* risk

Assessing peri-operative risk

- Risk of the surgery: renal transplant surgery is low-moderate
- Patient's risk based on their clinical status: most patients are intermediate
- Sometimes stress testing

Clinical Predictors of Peri-oprative Risk in the Patient

High	Intermediate
Recent MI,	ESRD / CKD
Unstable angina	DM
Decompensated CHF	
Severe valvular disease	
Severe arrhythmias	

CV Disease: Background

- Almost all patients have intermediate predictors of risk
- The transplant surgery is low-moderate risk

Therefore….

- The absolute rate of peri-operative MI is low (especially with appropriate use of beta-blockers)

Therefore….

- The benefit of generalized testing and interventions is likely limited

Which Test to Use ?

- Is it needed at all?
- Coronary angiography is gold standard but is invasive and in pre-dialysis patients, could precipitate contrast nephropathy
- ETT predicts risk in non-ESRD population but many ESRD pts don't achieve adequate 'stress'
- No consensus on the 'best test' in ESRD pts
- In practice, depends on your center

CV Assessment: A Practical Approach

- Assess pt for clinical predictors of peri-operative CV events
- If major clinical predictors of peri-operative risk: defer transplant
- Most will have 'intermediate clinical predictors' – consider a stress test (diabetics or known CAD or poor functional status)
- Reserve revascularization for standard indications
- Peri-operative beta-blocker if any CAD or any atherosclerotic CV disease

Peri-operative Management

- Intra-operative and post-operative beta-blocker; target HR 60-70
- Continue aspirin
- Common sense measures: avoid fluid overload, electrolyte abnormalities etc.

Optimizing CV status while on the list

- Control of HTN
- Control of CHF
- Rx of anemia
- Rx of hyperlipidemia ?
- Revascularization where appropriate
- Re-evaluate higher risk pts (eg diabetics) every 12m

The Diabetic Recipient

- Is whole organ pancreas (simultaneous or after kidney transplant) potentially of benefit?
- Timing of transplant
- CAD
- PVD
- Gastropathy (medications)
- Foot ulcers

Recurrent Disease

- Difficult to estimate as original dx may be unknown and recurrence is probably underdiagnosed post-transplant
- Histological recurrence ≠ clinical recurrence
- In 1 series, the third most important cause of graft loss (after rejection and death) in those with ESRD due to GN

Risk of renal allograft loss from recurrent glomerulonephritis; Briganti at al. N Engl J Med. 2002;347(2):103-9

Recurrent Disease

In general, transplant is not contra-indicated but should be deferred until the disease is quiescent

Idiopathic MPGN I, II and Membranous Nephropathy

- All may recur and all may be a/w allograft loss
- Important to exclude underlying causes such as HCV or TMA
- MPGN can resemble chronic transplant glomerulopathy on light microsopy
- Membranous Nephropathy can arise *de novo* after transplantation

SLE

- Allograft and pt survival same as non-SLE recipients (Ward; Kidney Int 2000 57:2136)
- Allograft survival poorer if superimposed APS
- Ensure disease clinically quiescent before transplant
- High steroid exposure: minimize further steroids; prevent osteoporosis etc.
- High prevalence of CV disease

Systemic (ANCA) Vasculitis

- Renal and extrarenal recurrence
- One series: recurrence anywhere in 17%; in graft in 10% (f/u mean 44m) Nachman et al, Kidney Int 1999; 56:1544
- Ensure disease is clinically quiescent before transplant
- ANCA at time of transplant probably not predictive of relapse
- Overall, allograft survival similar to non-vasculitis Magee et al, AST, 2003

Primary FSGS

- Circulating factor
- Recurs hrs – days;
- Proteinuria then ↑ Cr
- Risk factors: white, child, previous malignant course, recurrence in previous allograft
- Case series suggest benefit from plasmapheresis, high dose CNIs, steroids

HUS / TTP

- Many forms of HUS / TTP – essential to characterize in an individual pt
- Classic (diarrhea associated) – unlikely to recur but wait minimum 6 months
- Atypical (non-diarrhea) – likely to recur especially if inherited
- Prognosis if recurrence is poor

Atheroembolic Renal Disease

- Probably underdiagnosed as cause of ESRD?
- Most pts have significant comorbidities
- Potential for intraoperative atheroembolization to allograft
- Case reports of successful post-transplant outcomes

HIV

- No longer a C/I *per se*
- With HAART, survival of HIV+ (ESRD) pts has dramatically improved
- CNIs possibly have anti-HIV effects
- Short-term transplant outcomes encouraging
- Potential for multiple drug interactions

Advanced Age

- Age *per se* is no longer a C/I
- Selected elderly pts do better with transplant than remaining on the list

Johnson at al., Transplantation. 2000; 69: 794-9

- Rigorous screening especially for cancer
- Strongly consider *expanded criteria* donors
- Rejection may still be problematic

ABO-Incompatability

- Traditionally, very high risk of acute antibody mediated rejection and graft loss if transplant across ABO barrier
- Now, options include kidney exchanges or a plasmapheresis / immunosuppression protocol to remove antibodies

Highly Sensitized (to HLA antigens)

- Previous transplant or 'RBC' or pregnancy
- Traditionally: very long waiting times, higher rates of rejection and graft loss
- Excellent short-term outcomes with protocols involving either: high dose IgG or PP + IgG + MMF + tacrolimus
- Antibody mediated rejection still common but can be reversed
- Expensive, risk of overimmunosuppression

Conclusion

- Community nephrologists play a key role in the transplant process
  - Identification of patients who will benefit from transplant
  - Referral to the transplant center
  - Coordination of specialists in pretransplant evaluation
  - Continuation of care while waiting for transplant
    - Notifying transplant center of health status changes
  - Long-term care posttransplant