Case #1

- **37 year old** male, ESRD due to FSGS
- DD kidney transplant 5 years ago - primary nonfunction
- Second DD kidney transplant 3 years ago - massive proteinuria with recurrent *FSGS* 2 months post-transplant
- Back on dialysis 18 months later
- Wants another transplant (3rd)
Case #2

- **72 year old** Asian male, neuropsychiatrist, works full time
- ESRD due to FSGS, BMI 20.4
- HTN, CABGx5 vessel 10 years ago, on PD for 3 months, blood transfusion+, PRA: 40%
- **Prostate cancer**: diagnosed 8 months ago, Gleason score 7, treated with cryoablation, most recent PSA < 0.1
- Two potential donors: 58 yo friend and 24 yo grandson
Case #3

- 29 year old male, ESRD due to posterior urethral valves
- Kidney transplant from his mother at the age of 13 - lasted 7 years
- DD kidney transplant at the age of 22 - back on dialysis 14 months ago
- Multiple access surgeries - currently dialyzing via subclavian catheter
- Comes in for a 3\textsuperscript{rd} transplant - 8 hospital admission in the last 12 months for cocaine overdose and misses his dialysis treatments 2-3 times per month
Kidney Transplantation

- The **best** treatment option for majority of patients with ESRD regardless of sex, race, age or cause of ESRD
  - Increase in life expectancy
  - Increase in quality of life
  - Decrease in healthcare costs
- No formal upper age limit
- The demand for kidney transplantation exceeds the supply of transplantable organs
- Waiting times are quite long
What Makes Your Patient a Kidney Transplant Candidate?

• Is there a reasonable life expectancy?
• Can perioperative risk be reasonably managed?
• Does the patient have any condition(s) that will be worsened by, or complicate:
  - Surgery
  - Immunosuppression
• Is the surgery technically feasible?
Purpose of the Transplant Evaluation

• Identify potentially suitable recipients
• Prepare patients for kidney transplantation
  – Education of patients and families
    • Risks and benefits
    • Transplant options
  – Optimize candidate’s health
  – Help CKD planning for referring caregivers
Recipient Evaluation

- Referral for transplant evaluation-from nephrologists (majority) or self-referral (rare)
- Basic information gathering: insurance coverage, patient’s medical history, family history (including potential living donors) and laboratory results
- Initial interview and exam
Recipient Evaluation

- Physical exam
- Chest x-ray, ECG-12 lead
- Dental evaluation
- Pap smear, mammogram, PPD
- Labs: Complete metabolic panel, eGFR, CBC, serologies (HIV, hepatitis B and C, CMV, and RPR), HLA typing, PRA, PSA, blood type
Physical Exam

- Carotid pulse/bruit
- Peripheral pulses, abdominal and femoral bruit
- Careful abdominal exam: previous surgeries/scars, organomegaly, large kidneys in patients with PKD
  - *Is there enough room for the graft?*
- Testicular exam, rectal exam
- Breast exam
Recipient Evaluation

- Stress test (dobutamine echo or thallium)/echo/cardiac catheterization
- Colonoscopy
- Arterial Doppler of carotids or lower extremities
- CT abdomen/CT pelvis
- Toxicology screen
- Pulmonary function tests
- Bladder function
Age and Kidney Transplantation

- Growing population
- Above 70
  - Quality of life, NOT life expectancy
- Functionality with age
- Ethical issues
  - Organ shortage
  - Living donors
  - Age discrimination
- Case-by-case basis
  - Benefit vs risk of harm
Medical History

- Recent diagnosis of cancer
- Active infection (catheter-related, endocarditis, osteomyelitis, etc.)
- Recent chest pain, heart attack, or arrhythmias
- Foot ulcers, GI bleeding, blood transfusion
- Malnutrition, morbid obesity
Medical History-Cancer

• Active or recent evidence of a malignancy, except for some skin cancer (basal cell): transplant is contraindicated

• Israel Penn International Transplant Tumor Registry (IPITTR)

• Waiting time: varies amongst different tumors
  *Breast Ca*: at least 2 years-up to 5 years in certain tumors (regional lymph node involvement, bilateral disease, inflammatory histopathology)
Medical History-Cancer

• **Prostate Ca**: At least 2 years disease-free period followed by negative blind random biopsies
• **Renal cell Ca**: 2-year waiting time for asymptomatic >2 cm RCC, possibly shorter time <2 cm, at least 5 years for symptomatic RCC (recurrence risk is still ~26%)
• **Colorectal Ca**: waiting period of 5 years for all Duke’s classifications
Medical History - Infection - HIV

- Undetectable plasma HIV-1 RNA levels (viral load) for at least 3 months
- CD4+ T-cell count of more than 200 cells/microL
- No history of opportunistic infections or neoplasms (no AIDS-defining illness)
- Maintained on highly active antiretroviral therapy (HAART)
- Increased incidence of acute rejection after transplantation
- Close follow up – Infectious Diseases & Transplant Nephrology
Medical History-Infection
Hepatitis C

- The prevalence of the positive HCV antibody among HD patients in the US: average 9.3%, range: 6%-38% among dialysis centers
- Among the kidney transplant population, the prevalence of anti-HCV positivity range: 5%-46%, depending on the countries and/or centers
- Available data on kidney transplantation in this patient population suggest a survival advantage compared to remaining on hemodialysis
Medical History-Infection
Hepatitis C

• After transplantation, liver disease is more frequent in HCV-positive patients than in HCV-negative patients

• HCV-positive patients have a higher risk for developing proteinuria, diabetes and infections after transplantation

• Long-term patient and graft survival rates are lower in HCV-positive patients than in HCV-negative graft recipients
Medical History-Infection
Hepatitis C

- OPTN and SRTR database, Social Security Death Master File
- 75,629 HCV negative patients and 3,708 HCV positive patients, kidney transplant 1995-2004
- Increased mortality risk for HCV-positive recipients vs HCV-negative recipients, particularly among younger age groups
- The use of induction therapy was not associated with an increased mortality risk, for either lymphocyte depleting or nondepleting antibodies
- The use of MMF was associated with reduced mortality risk among HCV-positive recipients

Medical History-Infection
Hepatitis C

- All transplant candidates should be tested for HCV
- Serum transaminases may be normal even if the patient has advanced liver disease
- If HCV RNA is positive, proceed with liver biopsy
- Cirrhosis—consider combined liver/kidney transplant
- HCV is not a contraindication for transplant
Cardiovascular Disease

• Pre-transplant CVD is an important risk factor for post-transplant CVD
• High risk patients (diabetics, older patients, patients with 2 or more risk factors) should have a cardiac stress test/cardiac cath-if needed- before transplant
• Repeat screening every 1-2 years during waiting, every year for diabetics
Screening Diabetic Transplant Candidates for CAD

• Coronary angiography is recommended:
  - All Caucasian type I diabetics over age 45
  - Type I diabetics younger than age 45 with EKG changes (ST-T segment), smoking history (>5 pack/year), diabetes for at least 25 years

Sensitivity: 97%, negative predictive value: 96%

Obesity-Access to Kidney Transplantation

- 132,353 patients who were registered for kidney transplantation in the United States between 1995 and 2006
- Among all patients awaiting kidney transplantation, the likelihood of receiving a transplant decreased with increasing degree of obesity, categorized by ranges of BMI
- Similarly, the likelihood of being bypassed when an organ became available increased in a graded manner with category of obesity

Segev DL et al, JASN 2007
Registration for Kidney Waiting List, by BMI

% of new registrations

- BMI 35-40
- BMI >=40

Segev DL et al, JASN 2007
Obesity and Transplantation

- More superficial **wound** breakdown, complete wound dehiscence, and wound infections
- Similar graft survival and patient survival
  
  Johnson DW et al, Transplantation 2002

- UNOS data in obese (BMI 30-40) type 1 diabetic SPK recipients: **increased DGF, 1-year kidney acute rejection, and pancreas graft thrombosis**

- After adjusting for possible confounders, the odds ratios for overall **transplant complications** were 1.03 for overweight (BMI 25-29.9) and 1.38 for obese

- Obesity, but not overweight, was associated with patient death, pancreas graft loss, and kidney graft loss at 3 years

  Sampaio MS at al, Transplantation 2010
Obesity and Transplant Outcome

- UNOS database: 27,377 primary kidney-only transplants between 1997 and 1999
- Morbid obesity (BMI ≥ 35) was independently associated with increased risk of:
  - DGF (p < 0.001)
  - Prolonged hospitalization (p < 0.001)
  - Acute rejection (p = 0.006)
  - Decreased overall graft survival (p = 0.001)

Medical History-Other Risks

• Disease activity (lupus, vasculitis)
• Urologic disease, cystic disease
• Pre-transplant native kidney nephrectomy
• GI diseases (peptic ulcer, gallstones, pancreatitis)
• Medications (interactions)
• Psychosocial issues, alcohol and substance abuse
• Recurrent diseases (FSGS, MPGN, HUS, lupus)
• Ethical issues (noncompliance with medications, multiple transplants, transplant after recurrence)
What Can You Do to Help Your Patient’s Transplant Candidacy

• Encourage optimal health maintenance
  • Vaccinations
  • Exercise
  • Healthy eating
  • Adherence

• Keep transplant center “in the loop”
  • Records
  • Communication

• Refer early
  • Encourage pre-emptive transplant
Live Donor Evaluation
Living Donation-Facts

• The annual number of available deceased donors will not resolve the ongoing shortage of organs.
• The survival of a kidney transplanted from a live donor exceeds the results achieved from a deceased donor.
• Success of live donor transplantation no longer necessitates the consideration of an HLA match—unless there is possibility of a transplant from HLA identical sibling.
• The survival rate of a kidney transplant from a genetically unrelated donor is excellent.
Living Donors

• In 1954: Requiring an identical twin for success
• During the 1980’s: Selection of an HLA-matched family member
• Current: any person (irrespective of the HLA match) can be a donor if they are medically and psychosocially suitable
• It is illegal to buy or sell kidneys or coerce a donor
Potential Live Donor

• Appropriate for donation from nephrologic standpoint – what is his/her renal risk?
• Healthy enough for surgery?
• Competent, willing to donate; free of coercion
• Medically and psychosocially suitable
Potential Live Donor

- Fully informed of the risks and benefits of donation
- Fully informed of risks, benefits, and alternative treatment available to the recipient
- Ideally done by a separate group of nephrologists not involved in any way with the recipient’s care – free from bias
Potential Advantages of Live Donation

• Better short-term and long-term results
• More consistent early function and ease of management
• Avoidance of long wait for cadaveric transplant
• Less delayed graft function
• Less aggressive immunosuppressive regimens
• Surgery can be planned ahead (medical and personal convenience)
• Emotional gain to donor
• Helps relieve stress on national cadaver donor supply
Potential Disadvantages of Live Donation

- Psychological stress to donor and family
- Inconvenience and risk of evaluation process (i.e. IV contrast)
- Operative mortality (0.03% or 1 in 2000 patients)
- Major perioperative complications (4.4%, range: 0.0 to 13.0%)
- Minor postoperative complications (up to 50%)
- Long-term morbidity
- Risk of traumatic injury to remaining kidney
- Risk for unrecognized chronic kidney disease
Long-Term Consequences of Kidney Donation

- 3698 kidney donors who donated kidneys during the period from 1963 through 2007
- From 2003 through 2007: glomerular filtration rate (GFR) and urinary albumin excretion were measured; the prevalence of hypertension, general health status, and quality of life were assessed in 255 donors

Ibrahim H, et al. NEJM 2009
Long-Term Consequences of Kidney Donation

- The survival of kidney donors: similar to that of controls-matched for age, sex, and race or ethnic group
- ESRD developed in 11 donors: rate of 180 cases/million persons/year, as compared with 268 per million/year in the general population
- At a mean of 12±9 years after donation, 85.5% of the subgroup of 255 donors had a GFR of ≥60 ml/min, 32.1% had hypertension, and 12.7% had albuminuria
- Older age and higher BMI, but not a longer time since donation, were associated with both lower GFR (<60 ml/min) and hypertension

Ibrahim H, et al. NEJM 2009
Figure 1. Survival of Kidney Donors and Controls from the General Population.

I bars at 5-year intervals indicate 95% confidence intervals for the probability of survival among kidney donors.

Ibrahim H, et al. NEJM 2009
Long-Term Mortality

• Caucasian donors
  • No higher than demographically-matched individuals in the general population
    • Ibrahim et al. *NEJM* 2009.
    • Fehrman-Ekholm. *Transplantation* 1997

• All US donors (median follow-up 6 years)
  • No higher than demographically- and comorbidity-matched individuals in NHANES
    • Segev et al. *JAMA* 2010
Donor Evaluation

• Live kidney donor must receive a complete medical and psychosocial evaluation
• Blood typing: often the first test, relatively inexpensive
• Initial cross-match
• No transmissible diseases: HIV, HCV; HBV; no cancer
• Preliminary medical evaluation
Donor Evaluation

• Complete history (*hereditary dz) and physical exam
• Labs (routine, serologies, OGTT)
• UA, urine culture, pregnancy test
• 24 hour urine for protein and creatinine
• GFR measurement (glofil-ideal)
• Chest x-ray, ECG, exercise stress test for patients older than 50 years of age
• CT angio or MRA of renal arteries
• Psychosocial evaluation
• Repeat crossmatch before transplantation
Hereditary Diseases

- Alport’s syndrome
- Diabetes
- Polycystic kidney disease
- FSGS
- IgA nephropathy
- Hypertension
- HUS, SLE, and cystinosis
Alport Syndrome

- Defect in α5 subunit of type IV collagen in GBM
- Most cases X-linked recessive but in 15% are autosomal recessive
- Screen- urinalysis (UA), BP, hearing, eye exam
- Adult male with normal UA – can donate
- Adult female with normal UA – possible carrier
- Adult female with hematuria – definite carrier, cannot donate, 15% risk CKD
- Benign renal biopsy age >40, no HTN may consider them as donors
Diabetes

• Contraindication to donation
• Fasting plasma glucose >126mg/dl
• Fasting glucose 100-125mg/dl
  • Should have 2hr OGTT (>200 is c/w DM)
  • Consider for those with BMI>30, TG>250, HDL<35
• Family history of diabetes
  • 1st degree relative with DM – 25% risk of developing DM
  • 2 relatives with DM – 50% risk of developing DM
• Gestational diabetes requiring insulin
  • 50% risk of developing DM within the next 5 years
ADPKD

• Screen first degree relative donors with ultrasound
• Age specific ultrasound criteria for diagnosis
  • Age<30 – 1 cyst in each kidney or 2 cysts in 1 kidney
  • Age 30-59 – 2 or more cysts in each kidney
  • Age>60 – 4 or more cysts in each kidney
  • 100% reliable if donor >age 30
• DNA analysis is also available
• Use of MRI-might change the approach
Amsterdam Forum Guidelines

- A **GFR**<80 ml/min or 2 SD below normal (based on age, gender, and BSA corrected to 1.73 per m2) generally preclude donation
- Patients with a **BP**>140/90 mmHg by ABPM are generally not acceptable as donors
- Patients with a **BMI**>35 kg/m2 should be discouraged from donating (*BMI less than 30 at Upenn*)
- **Dyslipidemia** alone does not exclude kidney donation (Keep an eye on “Metabolic Syndrome”)

*Transplantation March 27, 2005*
Amsterdam Forum Guidelines

• A 24 h urine protein of >300 mg is a contraindication to donation

• Individuals with a history of diabetes or fasting blood glucose ≥126 mg/dl (7.0 mmol/l) on at least two occasions (or 2 h glucose with OGTT≥200 mg/dl (11.1 mmol/l) should not donate
Hematuria-Prospective Kidney Donors

- 512 consecutive prospective donors, 14 (2.7%) continued to have asymptomatic, microscopic hematuria over 1 month
- If the medical history, physical examination, and computerized tomographic angiography were unremarkable, and if they still wished to donate, a kidney biopsy was performed
- In two prospective donors, hematuria resolved after treatment for urinary tract infection
- Two others declined donation and were referred to their primary care provider

Koushik R, et al. Transplantation 2005
Hematuria-Prospective Kidney Donors

- Kidney biopsy in the remaining 10 showed: two normal; 4 thin basement membrane nephropathy (TBMN); one nonhomogeneous basement membrane abnormalities; one IgA nephropathy, one patient with 7 of 30 glomeruli globally sclerotic; and one TBMN and early hypertensive changes without systemic HTN.

- Only 4 of the 10 who underwent kidney biopsy donated (two normal, two TBMN).

Koushik R, et al. Transplantation 2005
Causes of Persistent Microscopic Hematuria

- **Glomerular** bleeding (common causes, not associated with proteinuria or casts)
  - Thin basement membrane nephropathy (TBMN)
  - Alport Syndrome (early stage) or carrier state
  - IgA nephropathy
Causes of Persistent Microscopic Hematuria

• **Extraglomerular** bleeding
  • Stone disease
  • Hemoglobinopathy (SS/SA hemoglobin)
  • Polycystic kidney disease
  • Benign prostatic hyperplasia (elderly donors)
  • Malignancy (bladder, kidney, prostate)
  • Arteriovenous malformations and fistulas
  • Schistosomiasis (in endemic areas)
  • Hypercalciuria, hyperuricosuria, etc.
Amsterdam Forum Guidelines

- Asymptomatic potential donor + history of a single stone may be suitable if:
  - No hypercalcuria, hyperuricemia, or metabolic acidosis
  - No cystinuria or hyperoxaluria
  - No urinary tract infection
  - No evidence of multiple stones or nephrocalcinosis on CT scan
Amsterdam Forum Guidelines

- **Stone** formers who should not donate are:
  - Nephrocalcinosis on X ray or bilateral stone disease
  - Stone types with high recurrence rates, and are difficult to prevent
Amsterdam Forum Guidelines

- A prior history of the following malignancies usually excludes live kidney donation:
  - Melanoma
  - Testicular cancer
  - Renal cell carcinoma
  - Choriocarcinoma
  - Hematological malignancy
  - Bronchial cancer
  - Breast cancer
  - Monoclonal gammopathy
So you think you can donate....

- Imaging
  - Verify 2 kidneys: no unilateral atrophy, no horseshoe kidney, no medullary sponge kidney
  - Vasculature – no FMD
- Kidney selection
  - Take the smaller kidney
  - Take the left kidney if possible
  - Fewest arteries/veins preferred
- Nephrectomy: usually laparoscopically
- Risk of death to donor ~1:3,500
- Medically complex donors
New Strategies in Living Donation

- New techniques: Hand-assisted laparoscopic donor nephrectomy
- Desensitization and transplantation across the blood-type barrier
- Older living donors for older recipients
- Paired kidney exchange (PKE)
- Altruistic (nondirected) donation
- Altruistic donor chains (domino paired donations)
- List exchange programs
- Living Donor Paired Donation program: increased since 2006 but makes up only 1% of transplants performed in the US
Paired Kidney Exchange

• To obtain compatible donor transplants for two or more recipients with immunologically incompatible potential live kidney donors by exchanging donors
• 2-way exchange or 3-way exchange-using a computer program-usually performed simultaneously
• PKE programs now operate in the Netherlands, South Korea, Romania, the United Kingdom, US and Australia
• Isolated reports of PKE have been published from Switzerland, Israel and Canada
• Most single centers are unable to enroll enough pairs for efficient exchange on a permanent basis, and collaboration with other centers is essential
Paired Kidney Exchange

- Legal framework to allow the development of national programs for both altruistic nondirected donation and paired donation
- Allocation algorithm for matching
- Mandatory medical suitability criteria
- Listing in the deceased donor waiting list
- Donor travel versus shipping of organs
Donor Evaluation-Actual Cases

- Microscopic hematuria and renal mass (renal cell carcinoma)
- Unknown pregnancy
- Significant bilateral hydronephrosis
- Horseshoe kidney
- Unrecognized hypertension
- Slightly elevated liver enzymes, + HCV (previously unknown)
- Fibromuscular dysplasia
- EF < 20% on ECHO
- Proteinuria: kidney biopsy IgA nephropathy
Case #1

- 37 yo male, ESRD due to FSGS
- DD kidney transplant 5 years ago - primary nonfunction
- Second DD kidney transplant 3 years ago - massive proteinuria with recurrent FSGS 2 months post-transplant
- Back on dialysis 18 months later
- Wants another transplant
- Listed for DD kidney transplant - inactive-accumulating time
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- **70 yo** Asian male, neuropsychiatrist, works full time
- ESRD due to FSGS, BMI 20.4
- HTN, CABGx5 vessel 10 years ago, on PD for 3 months, blood transfusion+, PRA: 40%
- **Prostate cancer**: diagnosed 8 months ago, Gleason score 7, treated with cryoablation, most recent PSA < 0.1
- Two potential donors: 58 yo friend and 24 yo grandson
- **Waiting time**: 2 years-listed
Case #3

- 29 year old male, ESRD due to posterior urethral valves
- Kidney transplant from his mother at the age of 13-aged lasted 7 years
- DD kidney transplant at the age of 22-back on dialysis 14 months ago
- Multiple access surgeries-currently dialyzing via subclavian catheter
- Comes in for a 3rd transplant-8 hospital admission in the last 12 months for **cocaine overdose and misses his dialysis treatments** 2-3 times per month
- Psychiatry to see; needs to complete rehabilitation program before he could be listed