

CORE CURRICULUM IN NEPHROLOGY

Evaluation of the Potential Living Kidney Donor

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Advances in immunosuppressive therapy and refinement in surgical techniques have allowed living donor transplantation to evolve from the first successful identical twin donor transplantation in 1954 to the current practice involving virtually all biologically related and unrelated medically and psychosocially suitable donors. During the past decade (1996 to 2006), the Organ Procurement and Transplantation Network/United Network of Organ Sharing (UNOS) database showed that although the number of deceased donors increased from 5,036 to 7,181, the number of living donors almost doubled from 3,681 to 6,434. The increased rates of living donation are believed to be caused in part by the superior patient and graft survival rates achieved with living compared with deceased donor transplantation, the advent of laparoscopic donor nephrectomy, and improved patient and public awareness. With the ever increasing disparity between donor organ supply and demand, the invaluable contributions from living donors are much needed.

Because living kidney donation for transplantation has become common practice, we must aim to protect both the potential donor and recipient from preventable or foreseeable physical and psychosocial complications. The following section provides general guidelines for evaluating a potential living donor candidate. Topics that must be discussed with the potential donor, including ethical, psychosocial, and financial issues, are outlined. A medical evaluation focusing on minimizing immediate cardiovascular and pulmonary risks and long-term medical risks to the donors, as well as transmittable malignancy and infection risks to the recipients, also is presented.

GENERAL ASSESSMENT

Mandatory preliminary evaluation of a potential living donor includes determination of blood group type A, type B, type O (ABO) compatibility, HLA typing, and cross-matching against the potential recipient. In cases in which more than 1 donor is available, selection of the best donor depends on the degree of HLA matching and

donor age. In addition, biologically related donors generally are preferred over unrelated donors. Although there are significant variations among transplant centers regarding the medical evaluation of living donors, the universal goals are to minimize immediate and future physical and psychosocial health risks to the prospective donor, as well as to the recipient. The major components involved in the evaluation of potential living donors are shown in Fig 1.

ETHICAL ISSUES

I. Source of donation

A. Paid donation

1. Illegal in the United States, Britain, Canada, Mexico, and all of Europe
2. In some countries, payment to the donors as compensation for their gift to the recipients may be allowed

B. Acceptable donations

1. Donors known to recipients
 - a) Related and unrelated donors, including spouses, friends, and acquaintances
2. Donors unknown to recipients
 - a) Altruistic donors (Good Samaritan or anonymous donors)
 - b) Paired kidney donation
 - (1) A program designed to match 1 incompatible donor/recipient pair to another pair with a complementary incompatibility

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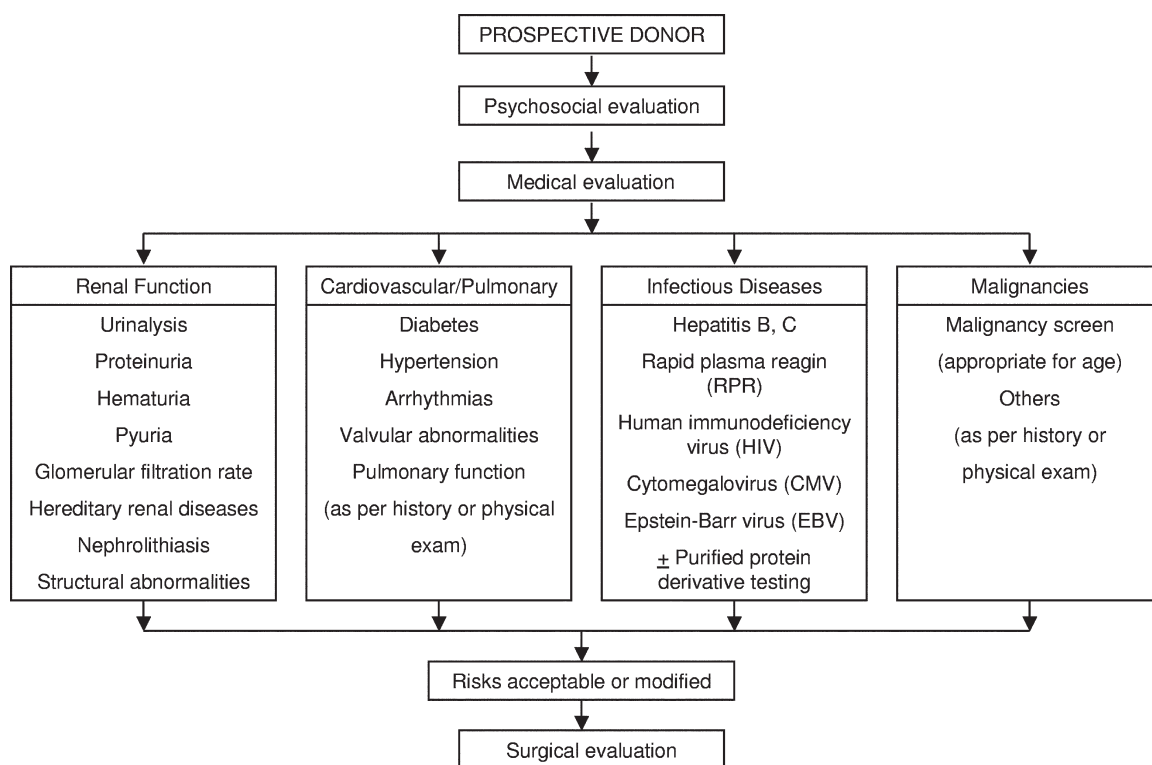


Figure 1. Major components involved in the evaluation of potential living kidney donors.

- C. Medical aspects of living donor evaluation are the same for all donor sources
- II. Protection of donors
 - A. Each donor should have an advocate (ie, a psychiatrist and nephrologist from the donor evaluation team) for unbiased advisory purposes with regard to the donation process
 - B. There should be separation of the recipient and donor teams
 - C. The physical and psychosocial well-being of the donor are of primary importance
- PSYCHOSOCIAL EVALUATION**
- I. Evaluation should be performed by a psychiatrist or mental health professional who has no personal and clinical relationship with the recipient
- II. Address protection of donor's confidentiality
 - A. Evaluation performed in the absence of recipient or recipient's advocates
- B. Use of translators unknown to recipient and donor
- III. Assess donor's accurate knowledge of
 - A. Recipient's health (physical and mental) benefits
 - B. Donor's health (physical and mental) risks
 - C. Donation process
- IV. Assess donor's motivation
 - A. Inform donor of option "not to donate" and ensure confidentiality
 - B. Exclude
 - 1. Coercion
 - 2. Secondary gain (monetary or other personal gain)
- V. Assess donor's ability to make decision
 - A. Evaluate sociodemographic history and current status
 - B. Evaluate underlying psychiatric disorders
 - 1. Stability
 - 2. Risk of recurrence after donation
 - C. Explore history of substance abuse

- D. Confirm full capacity to give informed consent
- VI. Assess adequacy of social and financial support
- VII. Discuss possible outcomes
 - A. Psychological benefits after a successful transplantation (increased self-esteem)
 - B. Resentment, depression after an unsuccessful transplantation
 - C. Discuss the possibility of covert depression with altruistic donor (unrelated, unknown, or anonymous donor) because donor may not witness and enjoy positive outcome

CARDIOVASCULAR EVALUATION

- I. Exclusion criteria as donor
 - A. Diabetes mellitus
 - B. Untreated and/or symptomatic coronary artery disease
 - C. Dilated cardiomyopathy
 - D. Compensated or decompensated heart failure
 - E. Untreated and/or symptomatic clinically significant arrhythmias
 - F. Untreated and/or symptomatic clinically significant valvular heart diseases
- II. Indications for cardiac structural evaluation with 2-dimensional echocardiogram
 - A. Abnormal cardiac murmurs
 - B. History of syncope, dizziness, palpitations, or shortness of breath
- III. Indications for Holter monitoring
 - A. Unclear history of arrhythmia
 - B. History of syncope, dizziness, or palpitations
- IV. Indications for cardiac stress testing (≥ 1 of the following or at the clinician's discretion)
 - A. Older age (ie, age > 45 years in men or > 55 years in women); may vary depending on donor's routine activity level
 - B. History of smoking
 - C. Family history of premature coronary artery disease
 - D. History of dyslipidemia (should be included in risk-factor assessment; dyslipidemia alone is not an indication for cardiac stress testing)
 - E. History of hypertension

- F. Abnormal electrocardiogram (ECG; left ventricular hypertrophy, left bundle branch block, ST-T abnormalities)

DIABETES MELLITUS

- I. Indications for oral glucose tolerance test (≥ 1 of the following)
 - A. Obesity
 - B. Potential donors with first-degree relatives with type 2 diabetes mellitus
 - C. History of gestational diabetes mellitus
- II. Absolute contraindications to donation
 - A. Known diabetes mellitus
 - B. Fasting plasma glucose (FPG) level of 126 mg/dL or greater (≥ 7.0 mmol/L) on 2 or more occasions
 - C. Plasma glucose level of 200 mg/dL or greater (≥ 11.1 mmol/L) 2 hours after 75-g oral glucose challenge (oral glucose tolerance test) on 2 or more occasions
- III. Relative contraindications to donation
 - A. Impaired fasting glucose (IFG), defined as FPG value between 110 and 125 mg/dL (6.1 and 6.9 mmol/L)
 - B. Impaired glucose tolerance (IGT), defined as 2-hour plasma glucose values between 140 and 199 mg/dL (7.8 mmol/L and 11.1 mmol/dL)
- IV. Individuals with IFG or IGT should be counseled on lifestyle modifications, including weight control, diet, exercise, and tobacco avoidance
- V. Prospective donors with IFG or IGT should be assessed on an individual basis
- VI. Donation not recommended in
 - A. Individuals with mild or borderline IGT and additional risk factors (first-degree relatives with type 2 diabetes mellitus, obesity, gestational diabetes mellitus, and dyslipidemia)
 - B. Individuals with blood glucose levels in the high range of IFG (110 to 125 mg/dL [6.1 to 6.9 mmol/L]) probably should not donate because of the greater tendency for deterioration
- VII. Prospective donors should be forewarned that both IFG and IGT are important predictive factors for progression to overt diabetes

HYPERTENSION

- I. Determination of blood pressure
 - A. Donors should have at least 2 office measurements documenting systolic blood pressure less than 140 mm Hg and diastolic pressure less than 90 mm Hg
 - B. For ambulatory blood pressure monitoring, donors should have a mean awake blood pressure less than 135/85 mm Hg and sleep blood pressure less than 120/75 mm Hg
- II. A positive history of hypertension may be acceptable for donation at some centers if
 - A. Prospective donor is non-African American
 - B. Aged older than 50 years who meet all of the following
 - 1. No evidence of end-organ damage
 - 2. Blood pressure is well controlled with lifestyle and behavioral modifications and/or use of no more than 1 antihypertensive
 - 3. Prospective donors must be followed up regularly with their primary care physician after donation
- III. A positive family history of hypertension is not a contraindication to donation

PULMONARY

- I. Pulmonary function testing for prospective donors
 - A. Not indicated routinely unless history or physical examination is suggestive of lung disease
- II. Moderate to severe pulmonary disease is a contraindication to living donation
 - A. Forced expiratory volume in 1 second (FEV_1) or forced vital capacity (FVC) less than 70% of predicted or $FEV_1:FVC$ ratio less than 65%
- III. Smoking cessation at least 4 weeks before the surgical procedure is advisable

RENAL FUNCTION

- I. Abnormal urinalysis results
 - A. Proteinuria
 - 1. Confirm with 24-hour urine collection
 - a) Collection performed in the absence of fevers, urinary tract infections, or intense exercise

- b) Rule out overcollection (suspect if total urine creatinine–body weight ratio > 25 mg/kg [>220 μ mol/kg], especially in those with low muscle mass)
 - c) Rule out undercollection (suspect if total urine creatinine–body weight ratio < 15 mg/kg [<132 μ mol/kg]; this is especially important in those with borderline high proteinuria)
 - d) Spot protein-creatinine ratios not recommended
 - (1) Minimal but clinically significant proteinuria may be missed
 - e) For proteinuria between 250 to 300 mg/d in those with no known renal disease risk factors, donation may be considered if urinary albumin excretion is negative
 - f) Otherwise, donation is contraindicated if confirmed proteinuria is greater than 250 mg/d
- B. Microscopic hematuria
 - 1. Rule out contamination from menstruating women
 - 2. Rule out urinary tract infections
 - 3. Evaluate for stones
 - a) Large stones: computed tomography (CT) urogram (routinely performed as part of CT angiogram; discussed next)
 - b) Microlithiasis: 24-hour urine for creatinine, calcium, oxalate, phosphate, uric acid, citrate, sodium
 - 4. Urology consultation to evaluate for urinary tract malignancy
 - 5. Renal biopsy if these results are negative to rule out glomerular diseases (ie, immunoglobulin A (IgA)/IgM nephropathy, Alport disease, thin basement membrane [TBM] disease), medullary sponge kidney, and significant hypertensive glomerulosclerosis
 - 6. Donation is contraindicated if
 - a) Evidence of glomerular abnormalities, especially in association with a strong family history of end-stage renal disease (ESRD) secondary to the same renal disease
 - b) Urinary tract malignancy
- C. Microscopic pyuria

1. Rule out urinary tract infections with urine culture and sensitivity
 2. Evaluate for prostatitis in men
 3. Rule out renal tuberculosis with 3 morning urine acid-fast bacilli cultures
 4. If all these are negative, consider renal biopsy to rule out interstitial nephritis or chronic pyelonephritis
 5. Donation is contraindicated if
 - a) Evidence of renal tuberculosis
 - b) Interstitial nephritis or pyelonephritis
- D. Abnormal glomerular filtration rate (GFR)
1. Measure creatinine clearance from a 24-hour urine collection
 - a) Preferred over the use of estimated formulas because data for proteinuria can be concurrently collected
 2. Decreased GFR less than 80 mL/min/1.73 m² (<1.33 mL/s/1.73 m²; or GFR < average age-specific GFR per the British Transplantation Society/Renal Association UK guidelines) is a contraindication to donation
 3. For those with borderline low GFR on a 24-hour urine collection, reassess with a nuclear study (eg, iodine 125 [¹²⁵I]-iothalamate, technetium 99m [^{99m}Tc]-diethylenetriamine)
- II. Abnormal renal imaging
- A. CT angiogram versus magnetic resonance imaging/angiogram (MRI/MRA)
1. Both are highly sensitive and specific
 2. CT has exposure to radiation
 3. CT is fast and can detect calcifications
 4. CT is better in defining renal vein anatomy than MRA
- B. Donation is contraindicated for, but not limited to, the following
1. Abnormal parenchyma
 - a) Significant unilateral renal atrophy or horseshoe kidney
 - b) Significant cortical scarring
 - c) Presence of 2 or 3 cysts in each kidney or complex or septated cysts
 - d) Angiomyolipoma
 2. Abnormal vasculature
 - a) Significant atherosclerotic disease
 - b) Fibromuscular dysplasia

- c) Donation is not contraindicated in cases with multiple renal veins or arteries
 - (1) Left versus right nephrectomy is determined by the surgical team based on the vasculature of both kidneys and ease and safety of the operation
3. Abnormal collecting system
 - a) Multiple stones or current single stone greater than 1.5 cm
 - b) Medullary sponge kidney

NEPHROLITHIASIS

- I. The routine evaluation of donors should identify any kidney stone
- II. A history of nephrolithiasis is only a relative contraindication
- III. For prospective donors with current stones or history of stones
 - A. Prospective donors with a distant history of a single stone (>10 years) without recurrence should be acceptable
 - B. Advise of increased risk of recurrence after diagnosis of first stone (risk of second stone is 50% in 5 to 7 years)
 - C. Lifelong annual evaluation for new stones in remnant kidney
 - D. Donation contraindicated if
 1. Abnormal metabolic evaluation (hypercalciuria, hyperuricemia, cystinuria, hyperoxaluria, hyperphosphatemia, hypocitraturia, metabolic acidosis, recurrent urinary tract infections)
 2. Nephrocalcinosis on imaging studies
 3. Bilateral stones
 4. Single stone greater than 1.5 cm

HEREDITARY RENAL DISEASE

- I. Autosomal dominant polycystic kidney disease (ADPKD)
 - A. Most commonly encountered hereditary renal disease
 - B. Diagnostic criteria are age dependent
 1. ADPKD1 diagnostic criteria (Ravine et al)
 - a) Younger than 30 years: 1 or more cysts per kidney or 2 or more cysts in 1 kidney

- b) 30 to 59 years old: 2 or more cysts per kidney
 - c) 60 years old: 4 or more cysts per kidney
 - 2. ADPKD2 may present later in life
 - a) Use of these ADPKD1 diagnostic criteria may lead to false-negative results
 - C. For prospective donors older than 30 years
 - 1. Safe to proceed if ultrasound or CT shows no evidence of cysts
 - D. For prospective donors between the ages of 20 and 30 years
 - 1. A negative ultrasound result does not rule out ADPKD
 - 2. Donation not recommended based on negative ultrasound screening alone
 - 3. Genetic studies (see below)
 - E. MRI
 - 1. Greater sensitivity in detecting smaller cysts
 - 2. Diagnostic criteria for ADPKD based on MRI have not been established
 - 3. May reliably exclude ADPKD at younger ages
 - 4. May lead to false-positive results
 - F. Genetic studies can more reliably exclude the presence of ADPKD
 - 1. Gold standard diagnostic test, but not routinely performed
 - 2. Linkage analysis
 - a) Rarely performed because of the requirement for testing of multiple affected and unaffected family members
 - 3. Direct DNA sequencing
 - a) May yield a definitive result less than approximately 70% of the time
 - b) For more information on ADPKD testing, refer to www.AthenaDiagnostics.com
 - 4. Safe to proceed if genetic testing excludes the presence of ADPKD
- II. Alport syndrome
- A. Predominantly X linked
 - B. Less commonly autosomal recessive or autosomal dominant
 - C. Prospective donors should be screened for
 - 1. Hematuria
 - 2. Hypertension
 - 3. Sensorineural hearing loss
 - 4. Ocular testing (anterior lenticonus, cataracts, retinal lesions)
 - D. Safe to proceed with donation if
 - 1. Absence of hematuria in an adult male 20 years or older
 - 2. Adult female siblings with normal urinalysis results
 - E. Donation not advised in female relatives with persistent hematuria because they are most likely carriers of the mutation
 - F. Genetic testing not yet readily available
- III. TBM disease
- A. Also known as benign familial hematuria
 - B. Usually autosomal dominant inheritance
 - 1. Screen first-degree relatives for hematuria
 - 2. Screen for hypercalciuria and hyperuricosuria
 - C. Must distinguish TBM disease from IgA nephropathy and Alport syndrome
 - 1. TBM disease
 - a) Gross hematuria in less than 10% of patients
 - b) Positive family history of hematuria
 - c) Typically negative family history of renal failure
 - 2. IgA nephropathy
 - a) Episodic gross hematuria relatively common (40% to 50%)
 - b) Family history of hematuria may occur in isolated cases
 - c) May have family history of renal failure
 - 3. Alport syndrome
 - a) May have episodic gross hematuria
 - b) Typically with positive family history of renal failure
 - c) Deafness may be present in families in which there is an X-linked mode of inheritance
 - D. Renal biopsy
 - 1. TBM disease and early Alport syndrome may be difficult to differentiate histologically

- E. Donation from individuals with TBM disease remains controversial
 - 1. The presence of hypertension, proteinuria, or both precludes donation
 - 2. Individuals with TBM disease may proceed with donation if
 - a) IgA nephropathy or Alport syndrome excluded
 - b) Age older than 40 years
 - c) Prospective donors must be counseled that although TBM disease typically has a benign outcome, slowly progressive renal insufficiency may occur
 - d) Long-term donor risk remains unknown
- F. Any effects of TBM disease on allograft function are unclear
- IV. Systemic lupus erythematosus (SLE)
 - A. Exclude familial SLE
 - B. SLE occurs in approximately 12% or more of first-degree relatives
 - C. Prospective donors should be screened for
 - 1. Antinuclear antibody (ANA)
 - 2. Complement levels
 - 3. Abnormal urinary findings
 - 4. Antiphospholipid antibody at the discretion of the clinicians (eg, individuals with history of deep vein thrombosis, stroke, pulmonary embolism, fetal loss, thrombocytopenia, hemolytic anemia, livedo reticularis)
 - D. Family member of a patient with SLE who has a positive ANA result precludes donation
- V. Familial primary glomerulonephritis
 - A. Should be considered when more than 1 family member is affected with renal disease
 - B. Familial IgA nephropathy
 - C. Familial idiopathic steroid-resistant focal segmental glomerulosclerosis
 - D. Familial membranoproliferative glomerulonephritis
 - E. Familial membranous nephropathy

MALIGNANCIES

- I. Malignancy screen (appropriate for age)
 - A. Colorectal cancer

- 1. Average risk: screening starting at age 50 years
- B. Breast cancer
 - 1. Screening starting at age 40 years
- C. Cervical cancer
 - 1. Papanicolaou smear and pelvic examination starting at age 18 years
- D. Prostate cancer
 - 1. Digital rectal examination and prostate-specific antigen (PSA) starting at age 50 years
 - 2. African American or family history of prostate cancer, screening at age 45 years
- E. In the presence of a family history of malignancy, screening should be performed at an earlier age at the discretion of the clinician
- II. The following history of malignancy generally precludes living donation
 - A. Melanoma
 - B. Renal or urological
 - C. Choriocarcinoma
 - D. Hematologic
 - E. Gastrointestinal
 - F. Lung
 - G. Breast
 - H. Monoclonal gammopathy
- III. History of malignancy (other than those mentioned)
 - A. Donation may be acceptable if the specific cancer is deemed cured and the potential for cancer transmission is excluded
 - B. Obtain oncology clearance

INFECTIONS

- I. In general, acceptable donors should have no evidence of chronic infections
- II. Screen all donors for human immunodeficiency virus (HIV), rapid plasma reagin (RPR), hepatitis B and C
 - A. Presence of HIV and hepatitis C are contraindications for donation
 - B. Presence of RPR requires evaluation for syphilis and treatment before further evaluation
 - C. Presence of hepatitis B surface antibody is not a contraindication for donation

- D. Presence of hepatitis B surface antigen is a contraindication for donation
- III. Screen for cytomegalovirus (CMV) and Epstein-Barr virus (EBV)
 - A. Past history of infection is not a contraindication for donation
- IV. Perform a purified protein derivative (PPD) skin test to screen for tuberculosis (at the discretion of the clinician based on history and physical examination and/or chest X-ray findings; the latter is routinely performed as part of the donor evaluation process); PPD skin test with control should be performed in all prospective donors coming from endemic areas

MISCELLANEOUS/OTHERS

- I. Absolute contraindications to living donation
 - A. Active infection
 - B. Significant chronic liver disease
 - C. Significant neurological disease
 - D. History of thrombotic disorders and presence of risk factors for future events (such as lupus anticoagulant, anticardiolipin antibody, abnormal activated protein C resistance ratio)
 - E. Disorders requiring anticoagulation
 - F. Current pregnancy
- II. Relative contraindications to living donation
 - A. Obesity: individuals with body mass index (BMI) greater than 35 kg/m² should be advised to lose weight and should not donate in the presence of other comorbid conditions
 - B. Jehovah's Witness adherents or individuals who refuse transfusion of blood products

FINANCIAL ASPECTS

- I. Discuss the economic impact with the prospective donor
 - A. Medical expenses
 - 1. Covered by recipient's insurance or, in certain circumstances, by the Transplant Centers Organ Acquisition Fund
 - 2. Donor evaluation
 - 3. Actual donation surgery
 - 4. Required postoperative care
 - B. Nonmedical expenses
 - 1. Not covered by recipient's insurance

- 2. Annual physicals
- 3. Travel
- 4. Lodging
- 5. Lost wages
- 6. Other nonmedical expenses
- II. Financial resources directory
 - A. (<http://www.transplantliving.org/beforethetransplant/finance/directory.aspx>)
- III. The act of donation should not preclude the donor from obtaining medical insurance or increase in insurance cost

POSTDONATION ISSUES

- I. Short-term issues
 - A. Activity restriction
 - 1. Heavy lifting or rough contact sports for 6 weeks
 - 2. May return to work by 4 weeks
 - 3. Restrictions may be lifted sooner for laparoscopic nephrectomy
 - B. Complete recovery may take 6 to 8 weeks
 - C. Incisional pain may be present for 2 to 3 months
- II. Long-term care
 - A. Medical evaluation by the primary care physician
 - 1. Annual evaluation
 - a) Frequency may be higher for those with other medical issues
 - b) Review of medications
 - (1) Advise to avoid all nephrotoxic agents, especially nonsteroidal anti-inflammatory agents and nephrotoxic herbal medications
 - c) Emphasis on maintaining healthy lifestyle
 - (1) Encourage
 - (a) Regular exercise
 - (2) Discourage
 - (a) High-protein high-salt diets
 - (b) Excessive weight gain
 - (c) Excessive alcohol consumption
 - (d) Smoking
 - (e) Use of recreational drugs
 - d) Blood pressure assessment

- (1) Maintain at less than 130/80 mm Hg
 - e) Routine chemistry tests, including serum sodium, potassium, serum carbon dioxide content, blood urea nitrogen, serum creatinine, and fasting glucose
 - f) Fasting lipid panel
 - g) Urinalysis
- III. Effects of unilateral nephrectomy
 - A. Deaths before discharge
 - 1. 0.03% (UNOS data between 1999 and 2002)
 - B. Short term
 - 1. Pain or discomfort
 - 2. Bleeding
 - 3. Infections
 - C. Long term
 - 1. Renal function
 - a) Proteinuria
 - (1) Marginal increase has been reported
 - (2) No apparent adverse clinical consequence in most patients
 - (3) Predonation borderline to mild proteinuria may incur increased risk of the development of significant proteinuria at long-term follow-up
 - b) Development of ESRD
 - (1) Current data generally show no evidence for worse incidence of ESRD compared with that of the general population
 - 2. Hypertension
 - a) Most studies reported no to minimal increased incidence of hypertension
 - b) Patients with mild hypertension do not appear to have an increased risk of more rapid progression of hypertension
 - 3. Pregnancy
 - a) No evidence for increased risk of infertility

- b) Pregnancy is not contraindicated, but should be delayed for at least 6 months to allow for maximal compensatory hypertrophy
 - c) No evidence of adverse outcomes with prenatal course
 - d) Must have early follow-up with a nephrologist
- 4. Life-span
 - a) Unchanged

ADDITIONAL READING

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