AJKD
Core Curriculum in Nephrology

# General Medical Care of the Dialysis Patient: Core Curriculum 2013

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*Note from Education Editor Scott Gilbert, MD: With this article, AJKD's Core Curriculum series, which provides readers with a basic analytical framework for approaching topics in clinical nephrology, changes from an outline to a narrative format. By using frequent headings and interspersed reading lists in a narrative presentation, the new format is intended to combine the convenient navigation of an outline with the clarity and flow of prose. As before, the feature is primarily intended for use by residency and fellowship program directors to develop educational programs.*

General medical care of the dialysis patient includes preventive care, health care counseling, and advance care planning. Because patients see their dialysis care providers regularly, coordinating medical care often falls to these clinicians. In some cases, for example, advance care planning, conditions of coverage under the US Centers for Medicare & Medicaid Services mandate that dialysis units and nephrologists provide some aspects of general medical care. Unique aspects of end-stage renal disease (ESRD), such as transplantation candidacy and high mortality, influence the appropriateness of some types of general medical care that will differ from the nondialysis population. This Core Curriculum outlines topics in preventive care, health care counseling, and advance care planning relevant to the care of dialysis patients. Because advance care planning depends on the competence of the patient, cognitive impairment and depression screening also are reviewed briefly. General medical care issues directly related to dialysis, for example, cardiovascular risk factors and specifics about bone and mineral metabolism, are not addressed in this Core Curriculum, but have been reviewed in other Core Curricula. An outline of topics covered, which could be treated as a rounding checklist, has been provided in Box 1.

## PREVENTIVE CARE

### Immunizations

#### *Overview*

Immunization is an integral aspect of general medical care in dialysis patients. Dialysis patients exhibit a reduced response to immunizations and develop lower antibody titers and less sustained antibody responses. It is postulated that alterations in T lymphocytes and antigen-presenting cells are responsible for the impaired immunity. Nevertheless, the Centers for Disease Control and Prevention (CDC) recommends vaccinating dialysis patients, in part because in theory, patients may be effectively protected from infection despite low levels of measured antibodies, but also because the vaccinations limit transmissions of the virus in dialysis units. Altering immunization schedules, increasing vaccine doses, and adding adjuvants that attract antigen-presenting cells to the vaccination site and thereby stimulate cellular and humoral responses to immunization are all used to increase the immune response in dialysis patients. A beneficial synergistic effect of dual vaccination, noted with simultaneous tetanus and hepatitis B vaccination and pneumococcal and influenza vaccination, also has been observed.

Table 1 lists the recommended immunizations for dialysis patients based on age and transplantation candidacy. Administering live vaccines is contraindicated in immunosuppressed and transplantation patients; therefore, any live vaccines indicated based on clinical circumstances (intranasal influenza, varicella, zoster, measles, mumps, rubella, yellow fever, BCG, and oral *Salmonella typhi*) should be given prior to transplantation despite the potential problem of impaired immunity.

#### *Hepatitis B Vaccine*

Hepatitis B, a human viral pathogen transmitted by percutaneous inoculation through an exchange of contaminated blood, blood products, or body fluids, was responsible for outbreaks of infection in hemodialysis units in the 1970s and 1980s. Since that time, hepatitis B vaccination has been recommended for all dialysis patients. Only 34%-88% of dialysis patients develop seroprotective antibodies to hepatitis B, even when higher vaccine doses are administered. Improved, although variable, antibody response has been shown with vaccine manipulations, including intradermal injections, adjuvants, coadministration of immunomodulators, and combining hepatitis B and A vaccines. Current recommendations include administering

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**Box 1.** Overview of General Medical Care Issues in Dialysis Patients

**Preventive Care**

- Immunizations
  - ◇ Hepatitis B
  - ◇ Influenza
  - ◇ H1N1
  - ◇ Tetanus
  - ◇ Pneumococcal
  - ◇ Human papilloma virus
  - ◇ Varicella zoster
- Hearing and vision
- Dental
- Falls
- Frailty

**Health Care Counseling**

- Exercise
- Obesity and weight loss
- Alcohol use
- Tobacco use and cessation
- Contraception and sexual dysfunction

**Screening**

- Cancer
- Cognitive impairment
- Depression

**Advance Care Planning**

- Resuscitation status
- Designated surrogate decision maker
- Physician orders for life-sustaining treatment (when applicable)

an increased vaccine dose (40 $\mu$g) 3 or 4 times depending on which vaccine formulation is used. Patients who respond but lose antibodies over time should be given a booster vaccine. Patients who do not respond to an initial vaccine series should be administered an additional series in an attempt to induce a response. Subsequent vaccination strategies are unclear, as is the schedule for obtaining antibody levels. Vaccinating patients early in the course of their chronic kidney disease (CKD) is recommended because improved antibody production is seen in those with less severely decreased kidney function. Therefore, hepatitis B vaccination should be included in CKD care and not delayed until the initiation of dialysis therapy. Table 1 outlines the recommendations for hepatitis B vaccination in dialysis patients.

### *Influenza and H1N1 Vaccines*

As with other vaccines, dialysis patients develop variable responses to influenza vaccination, with 36%-90% of patients developing protective antibodies. Patient factors, as well as differences in the antigen immunogenicity of seasonal vaccines, likely account for the variability. Similarly, response rates to H1N1 vaccination vary among dialysis patients, ranging from 33%-64%. No serious adverse effects from the H1N1 vaccines have been observed. Because complications of influenza infection (notably hospitalization and development of pneumonia) are believed to be more common in dialysis patients and mortality from H1N1 infection is as high as 5% in dialysis patients, it has been recommended that dialysis patients receive the influenza vaccine yearly. However, conventional analyses examining vaccinated versus unvaccinated groups are prone to bias. A recent study looking at influenza illnesses, morbidity, and mortality that compared years using vaccines matched to circulating virus with a year in which a mismatched vaccine was used suggested only a small benefit of current influenza vaccine in dialysis patients. The authors suggested that it is premature to abandon yearly influenza vaccination in dialysis patients, but that alternate vaccination strategies to improve effectiveness (use of adjuvants, high vaccine doses, etc) should be investigated. Depending on the vaccine potency and adjuvant cost, administering adjuvanted influenza vaccines to all adult hemodialysis patients may be cost-effective.

### *Tetanus, Pneumococcal, Varicella Zoster, and Human Papilloma Virus Vaccines*

There are a few isolated studies examining dialysis patients' responses to tetanus and pneumococcal vaccination. As occurs with other vaccines, antibody development and maintenance are reduced in dialysis patients, but until there are more specific studies on

**Table 1.** Recommended Adult Immunization Schedule for US Dialysis Patients

| Vaccine | Notes |
|---|---|
| Influenza | Age ≥19 y, 1 dose trivalent vaccine annually |
| Tetanus, diphtheria, pertussis | 1-time dose of Tdap then boost with Td every 10 y |
| Varicella | 2 doses if no evidence of immunity |
| Human papillomavirus | Female: 3 doses through age 26 y; male: 3 doses through age 21 y |
| Zoster | Age >60 y, 1 dose |
| Measles, mumps, rubella | 1 or 2 doses if no evidence of immunity |
| Pneumococcal | 1 or 2 doses |
| Hepatitis B | 40 $\mu$g of Recombivax HB on 3-dose schedule or 2 doses of 20 $\mu$g of Energix B on 4-dose schedule |
| Meningococcal | Only if other risk factor is present |
| Hepatitis A | Only if other risk factor is present |

*Note:* Based on Centers for Disease Control and Prevention Recommended Adult Immunization Schedule (http://www.cdc.gov/vaccines/schedules/downloads/adult/mmwr-adult-schedule.pdf), where further dosing information is available.

the frequency of diseases that theoretically could be prevented by immunizing dialysis patients (as well as on the morbidity and mortality attributable to those diseases), the CDC recommends that all dialysis patients receive these vaccines (Table 1). A second dose of pneumococcal vaccine should be given 5 years after the initial dose if the patient was younger than 65 years at the time of the initial vaccination. Repeated vaccinations are not advised due to the risk of developing immune tolerance. Outcome data are sparse, but one study suggested a small but significantly reduced mortality (hazard ratio, 0.73; 95% confidence interval, 0.68-0.78) in the 21% of 118,533 maintenance hemodialysis patients who received pneumococcal vaccination with or without influenza vaccine. In 2005, a tetanus, diphtheria, and acellular pertussis vaccine was licensed for use in the United States for those aged 11-64 years. A single booster dose of this vaccine is suggested for adults and may be given 2 years or less after the last tetanus vaccine in high-risk people.

There is no information about varicella or human papillomavirus vaccines in dialysis patients. For dialysis patients on transplant waiting lists, the CDC recommends that appropriate individuals (women aged <26 years, girls aged 11-12 years, and probably also boys aged 11-12 years) receive a human papillomavirus vaccine. Varicella zoster infection is common in immunosuppressed and elderly individuals and may affect solid-organ transplant recipients. Because it is a live virus, it is contraindicated in immunosuppressed individuals. Some have suggested that potential kidney transplant recipients who have some immunity to varicella by antibody titer measurement be considered for varicella zoster immunization. However, there are no data for the efficacy and safety of this vaccine in dialysis patients.

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## Cancer Screening

Adult periodic health examinations typically include age- and sex-appropriate cancer screening. Recommendations for cancer screening are based on disease occurrence, risks of screening, sensitivity and specificity of screening tests, and ultimately, the reduced mortality observed if screening detects disease. Thus, the expected survival of the individual to be screened is an implicit aspect of cancer screening. The high mortality in dialysis patients makes routine cancer screening inappropriate for this population. Cost-effective cancer screening in dialysis patients depends on the patient's risk of developing the cancer (including his or her personal cancer risk factors), expected survival, and transplantation status. Hypothetical analyses have determined that typical cancer screening (for cervical, colon, breast, and prostate cancers) in dialysis patients would result in 5 or fewer days of life saved. Cancer screening in these analyses is least effective in dialysis patients who are aged 50-70 years, women, and/or white.

Some cancers occur more frequently in the dialysis population, notably viral-mediated and urologic cancers. Acquired renal cystic disease also is more common in dialysis patients and is associated with a small

**Table 2.** Cancer Frequency in the ESRD Population

| Cancer | Standardized Incidence Ratio | Risk Factors |
|---|---|---|
| Renal cell | 3.6-24.1 | Acquired cystic disease |
| Bladder and ureter | 1.5-16.4 | Analgesic abuse, Balkan nephropathy, oral cyclophosphamide |
| Multiple myeloma | 4.0 | — |
| Cervical, uterine | 2.7-4.3 | Human papillomavirus |
| Liver | 1.4-4.5 | Hepatitis B and C |
| Thyroid & other endocrine organs | 2.3 | — |
| Tongue | 1.9 | Human papillomavirus |
| Prostate | 0.9-2.1 | — |

**Box 2.** Cost-Effective Cancer Screening in Dialysis Patients

**Breast**

- Mammogram yearly at age >40 and on transplant waiting list
- Clinical breast examination yearly at age ≥40; every 3 y for those in 20s-30s
- Screening in high-risk individuals with long expected survival

**Cervical**

- Yearly Papanicolaou test ~3 y after beginning vaginal intercourse and no later than age 21; newer liquid-based Papanicolaou test can be done every 2 y
- Consider testing for HPV DNA and administering HPV vaccine, especially in transplantation candidates
- Yearly Papanicolaou test in those on transplant waiting list and those with risk factors and long expected survival

**Colon and Rectal**

- Starting at age 50 in average-risk patients, stool-based test, flexible sigmoidoscopy, or optical colonoscopy for those on transplant waiting list
- No screening over age 75 or life expectancy <10 y
- Screen high-risk individuals with long expected survival

**Renal Cell**

- Yearly CT or MRI in patients on dialysis >3 y and on transplant waiting list

**Prostate**

- Annual PSA and digital rectal examination beginning at age 50 for men on transplant list

Abbreviations: CT, computed tomography; HPV, human papillomavirus; MRI, magnetic resonance imaging; PSA, prostate-specific antigen.

incidence of renal cell adenocarcinoma. However, ultrasound or computed tomographic screening all dialysis patients for renal cell carcinoma is not cost-effective. Breast and colon cancer are not more common in dialysis patients. Table 2 lists cancer frequencies in dialysis patients based on registry studies. With the exception of prostate cancer, dialysis patients are not more likely to be given a diagnosis of late-stage cancers. Box 2 summarizes the recommendations for cancer screening in dialysis patients. In general, individualized decisions will direct appropriate cancer screening. Patients on transplant waiting lists and those with long expected survival will require more routine screening.

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## Hearing and Vision

### *Hearing*

Sensorineural hearing loss occurs significantly more often in dialysis patients than in the general population, occurring in 46%-77% of these patients. Higher rates of hearing loss occur in both children and adults treated with dialysis, although some have found less hearing loss in peritoneal dialysis patients compared with those on hemodialysis therapy. The kidney and cochlea share physiologic processes involving the active transport of fluid and electrolytes (by the glomerulus in the kidney and the stria vascularis in the cochlea). This function may account for the similar effects of some medications (eg, aminoglycosides), diseases such as vasculitis, and hereditary conditions such as Alport syndrome on the kidney and hearing. Etiologic factors that contribute to hearing loss in dialysis patients include electrolyte disturbances, hypertension, exposure to radiocontrast, use of ototoxic medications, and possibly vitamin D and nerve conduction dysfunction. The hearing loss is primarily in the high frequencies and is not related to duration of ESRD or blood measurements such as serum urea nitrogen, creatinine, electrolyte, or hematocrit values. Some patients show retrocochlear auditory abnormalities (measured by brainstem audiometry). Vestibular dysfunction also has been reported in dialysis patients, especially those exposed to high total doses of aminoglycosides. Periodic auditory testing is recommended for all dialysis patients as part of general medical care depending on clinical status and results of screening for hearing loss.

The primary treatment for hearing loss is amplification by hearing aids. However, significant barriers to hearing aid use exist, including accepting the need, selecting and purchasing the device, and getting used to the device. For dialysis patients, there are the added issues of scheduling appointments around dialysis treatments and, for some, the cost, because Medicare does not cover the cost of hearing aids. There is little information showing improvement in overall quality of life with hearing aids, but hearing and hearing-related quality of life are positively affected. Integrat-

ing hearing assessment into the overall health care of dialysis patients may lead to better treatments and outcomes.

### *Vision*

Compared with the general population, individuals with CKD are affected more commonly by ocular diseases, including cataracts, subconjunctival calcification, optic neuropathy, microvascular and diabetic retinopathy, and macular degeneration. Because the inner retina and glomerular filtration barrier share developmental pathways, capillary networks, and structural features, retinal disorders characterize a number of inherited kidney disorders. These include retinitis pigmentosa with nephronophthisis, drusen with Alport syndrome and dense deposit disease, crystal deposits with oxalosis and cystinosis, and vascular abnormalities with Fabry disease. Vision-threatening retinal abnormalities, such as diabetic and microvascular retinopathy and macular degeneration, also are more common in dialysis patients. Regular ophthalmologic monitoring may prevent complications such as retinal detachment or hemorrhage. Routine screening may detect retinopathy and macular degeneration, treatment for which may delay the loss of vision. Thus, all dialysis patients should undergo regular ophthalmologic examinations. Diabetic patients in particular should continue to have regular examinations for retinopathy; per the USRDS (US Renal Data Systems) annual data reports, this is an area of general medical care that deserves attention and improvement.

Heparin anticoagulation during the hemodialysis procedure is considered safe; there appears to be no increase in retinopathy in hemodialysis patients receiving heparin compared with patients on peritoneal dialysis therapy. Although recent information suggests that significant changes in ocular perfusion pressure and intraocular pressure do not occur during normal hemodialysis treatments, there are cases in the literature of worsening intraocular pressure in patients with glaucoma who are undergoing hemodialysis. The rarity of this event necessitates communication between nephrologists and ophthalmologists. Mannitol and acetazolamide may be used, and one case report suggests that nocturnal home hemodialysis may be an effective therapy.

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## Dental Health

A variety of dental conditions are more common in CKD and dialysis patients than in the general population. These include periodontal disease, enamel abnormalities, narrowing of the pulp chamber, premature tooth loss, and xerostomia. In addition, the salivary glands, bone, mouth cavity, tongue, and temporomandibular joint may be affected by CKD and its complications. Consequences of poor dental health may include increased mortality and systemic inflammation (associated with periodontal disease), protein-energy wasting (attributed in part to poor oral intake and inflammation associated with periodontal disease), and atherosclerotic complications (as a result of increased inflammation primarily due to periodontal disease). Manifestations of renal osteodystrophy in the mandible, maxilla, and oral cavity may include demineralization, metastatic soft-tissue calcifications, tooth mobility, malocclusion, enamel hypoplasia, and pulp stones. Retrograde parotitis also appears to be more common in patients with CKD, likely as a result of direct gland involvement, chemical inflammation, dehydration, mouth breathing, and side effects of medications. Xerostomia, or dry mouth, may predispose to caries and gingival inflammation, as well as contribute to problems with dental retention, mastication, speech difficulties, dysphagia, sore mouth, infection, and loss of taste. Reduced salivary flow may be caused by medications (antidepressants, antiemetics, antihistamines, antipsychotics, and antihypertensives, notably $\beta$- and $\alpha$-blockers and diuretics) and increasing age.

Gingivitis and periodontitis (inflammation of the gingiva and supporting tissues of the teeth) are common manifestations of poor dental health and occur more frequently in dialysis patients. Periodontitis is a potential source of inflammation because organisms colonize periodontal pockets, which recruits inflamma-

tory cells, leading to secretion of proinflammatory mediators. Some have suggested that periodontitis therefore may contribute to higher dialysis patient mortality and cardiovascular disease through inflammatory pathways. Atherosclerotic vascular disease and periodontal disease have several risk factors in common, such as cigarette smoking, age, and diabetes mellitus. Observational studies indicate that atherosclerotic vascular disease and periodontal disease are associated independently of known confounders, but a causal relationship is not supported to date.

The cause of periodontitis in dialysis patients is not clear, but disturbed humoral defenses and repeated anticoagulation with heparin, which may predispose to gingival bleeding and consequent bacterial colonization, have been postulated. In addition, routine dental care (flossing, brushing, use of mouthwashes, and preventive care by dentists) is less common in dialysis patients. Tooth brushing, flossing, and mouthwashes may reduce gingivitis. Regular dental hygiene care with mechanical debridement and surgery when needed may prevent the start and progression of periodontal disease. Xerostomia can be reduced by avoiding mouth breathing; using a humidifier; avoiding use of tobacco, alcohol, and/or mouthwashes containing alcohol; and using saliva substitutes and sugar-free gum to stimulate salivary flow. Avoiding medications that contribute to dry mouth also may be helpful. Calcium channel blockers can cause gingival hyperplasia and thereby contribute to periodontal disease; therefore, their use should be limited in select patients. For dialysis patients, being aware of the importance of dental health may lead to fewer dental complications and possibly reduce opportunities for systemic inflammation.

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### Falls Assessment and Fractures

Fractures occur in 10%-40% of dialysis patients and ~50% of dialysis patients older than 50 years. Hip fractures are 4 times more frequent in dialysis patients and increase mortality substantially. The complex abnormalities of bone and mineral disorders in CKD contribute to inadequate understanding, diagnosis, and management of this problem. For example, bone density measurements in the general population predict fracture risk, but bone density in dialysis patients has limited fracture prediction. In patients with CKD stages 4 and 5, bone mineral density of the hip and radius generally are lower than in the general population, but in the lumbar spine, it is similar. Bone density also does not predict the type of renal osteodystrophy. There are no longitudinal studies of bone mineral density in patients with CKD, and the association of parathyroid hormone and bone mineral density is variable in CKD. For these reasons, routine bone density testing is not recommended in dialysis patients. However, the high frequency of hip fractures in dialysis patients and their associated high mortality argue for some identification of those at risk. Risk factors for hip fracture in dialysis patients include increasing age, female sex, white race, lower body mass index, lower serum albumin level, cardiovascular disease, peripheral vascular disease, and dependence on assistance for ambulation or transfers. Few of these factors are modifiable, but because most hip fractures are preceded by a fall, identifying dialysis patients at risk for falls and intervening to reduce the fall risk is a reasonable management strategy.

Falls are more common in dialysis patients and account for a significant proportion of dialysis unit–related adverse events. Although community-dwelling older adults generally experience 0.6-0.8 falls/patient-year, a rate of 1.6 falls/patient-year has been reported in older dialysis patients. Risk factors for falls in dialysis patients include age, comorbid conditions, mean predialysis systolic blood pressure, and a history of falls. Unlike the nondialysis population, number of medications, and specifically psychoactive medications, has not been associated with fall risk in dialysis patients. The dialysis procedure itself may contribute to falls through dialysis-associated hypotension, arrhythmias, and postdialysis fatigue. Asking patients about falls will identify those at higher risk (previous fall is a risk for subsequent falls), as will a simple assessment of impaired mobility. An easy screen for impaired mobility is to observe the patient rise from a chair, walk, and sit down again. More formal testing may involve a quantitative fall assessment. Patients with impaired mobility may be candidates for formal assessment of fall risk, including a home visit and physical and occupational therapy evaluations. Assessing vision, hearing, and muscle strength may be important components of evaluating fall risk. Because vitamin D supplementation has been associated with a reduction in falls, evaluation of 25-hydroxyvitamin D levels and supplementation in

patients with low levels may reduce fall risk. Exercise training to improve muscle strength also may reduce fall risk in dialysis patients. Simply making dialysis unit staff aware of the risk and complications of falls may promote preventive interventions in the dialysis unit.

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### Frailty

The frailty phenotype initially was described in the geriatric population, in which it predicts disability, hospitalization, and mortality. The original definition of frailty required the presence of 3 or more criteria, including weight loss, muscle weakness, fatigue or exhaustion, low physical activity, and slow gait. Subsequently, the Women's Health Initiative observational study, which used a simplified definition based on the standard quality-of-life 36-Item Short Form Health Survey (SF-36) questionnaire, found frailty to be associated with death, hip fractures, hospitalization, and reduced ability to complete activities of daily living. In the Dialysis Morbidity and Mortality Wave 2 Study, which used patient questionnaires to identify frailty in 2,275 hemodialysis patients, 67.7% of patients met the frailty criteria (44% of patients aged <40 and 66% of those aged 50-60 years). Frailty was more common in women, those with comorbid conditions, hemodialysis patients, and older patients. Frail patients were more likely to be hospitalized and to die within the year. Although the concept of frailty as an outcome predictor is relatively novel, it is recognized as a clinically useful expression of complex cumulative stresses on a biologic model leading to functional decline. Thus, identifying frailty in dialysis patients could lead to early interventions with the goal of avoiding or forestalling functional decline and therefore hospitalization and possibly death.

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## HEALTH CARE COUNSELING

### Exercise

The potential benefits of exercise include improved physical functioning, blood pressure and diabetes control, enhanced psychological well-being, and cardiovascular risk reduction. Therefore, exercise potentially can enhance health-related quality of life. Despite the number of positive effects of exercise on general health, dialysis patients generally are inactive, with only 13% reporting the recommended level of physical activity (moderate-intensity activity 3 d/wk, 30 min/session). Nephrologists rarely assess patients' physical activity or counsel patients about the benefits of exercise; only 38% of nephrologists "often" or "almost always" assessed dialysis patients' physical activity according to a 2003 survey of 505 nephrologists. Barriers to physical exercise that dialysis patients experience include fatigue and shortness of breath, as well as lack of time and motivation.

Early studies of exercise in dialysis patients focused on cardiovascular outcomes and typically examined the effects of aerobic exercise on peak oxygen consumption. Most were short-term studies (8 weeks to 6 months) and a 17% improvement in peak oxygen consumption was a typical finding, although there was significant variability. These trials found that even after training, dialysis patients failed to reach the peak oxygen consumption achieved by nondialysis patients. Importantly, looking at results of several small studies in aggregate, despite the improvement in peak oxygen consumption, no consistent gains in physical functioning, physical performance, or quality of life have been observed. Similarly, these studies suggest that most dialysis patients fail to show improvements in anemia, mental health, and lipid metabolism with exercise, although this observation again is limited by the small numbers of participants. In contrast, blood pressure control was improved in 2 studies of dialysis patients enrolled in exercise programs. It is possible that exercise during dialysis may improve small-solute removal by a greater efflux of urea into the vascular compartment created by increased muscle blood flow during exercise. Several small studies have shown increased urea removal with exercise, but this

benefit may be counteracted by reduced exercise tolerance during dialysis.

The largest study of exercise in dialysis patients, the Renal Exercise Demonstration Project, focused on physical performance and health-related quality of life rather than peak oxygen consumption. In this study, 286 patients underwent 8 weeks of home-based training followed by 8 weeks of cycling exercise during hemodialysis treatments. Patients were encouraged to reach a goal of 30 minutes of cycling per hemodialysis session and walking, cycling, and flexibility and strengthening exercises at home 3-4 times per week. Physical performance and health-related quality of life improved 12% in study patients compared with nonexercising controls. The most improvement was seen in patients with the lowest functioning at baseline. Subsequent smaller studies showed improvements in muscle strength and fatigability with cycling exercise during dialysis.

The ability to monitor adherence, the regular recurrence of sessions, and the relative practicality of setting up equipment in the hemodialysis setting has led many to initiate exercise programs during dialysis sessions. With warm-up periods and a gradual increase in exercise intensity, risks of exercise during dialysis are minimal; no cardiovascular events have been reported in published studies of dialysis exercise programs. There are no guidelines addressing medical screening for enrollment in dialysis-based exercise programs. The nephrologist should consider whether patients with symptoms of or known cardiac disease should undergo exercise testing before beginning a vigorous exercise program. The necessity for preexercise testing will be dictated in part by the proposed intensity of the exercise. Current studies are examining the effects of exercise on markers of inflammation, endothelial function, and vessel distensibility and may offer future insights into the pathophysiology of cardiovascular and nutritional abnormalities associated with CKD, as well as the effects of exercise on dialysis patients' morbidity and mortality. Available information suggests that exercise can improve dialysis patients' physical functioning, including fitness, muscle mass, physical performance, and self-reported physical functioning. Such improvements should reduce the risk of frailty and functional dependence. The success of a dialysis unit exercise program depends on assessment of patients' exercise practices and staff encouragement and dedication to the program.

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### Obesity and Weight Loss

As in the general population, obesity is an increasing problem in dialysis patients. In this population, in the United States, mean body mass index has increased from 25.7 kg/m$^2$ in 1995 to 27.5 kg/m$^2$ in 2002; a total of 30% of dialysis patients are obese. Although obesity may offer a survival advantage in hemodialysis patients, it can be a barrier to kidney transplantation and is a known complication of peritoneal dialysis. There is limited information about the treatment of obesity and the effectiveness of weight-loss strategies in dialysis patients. Behavior and dietary modification with or without exercise generally provides modest weight loss that can be maintained successfully, but requires long-term commitment. Dialysis patients face additional barriers due to their dietary restrictions and inability to use noncaloric liquid intake to alleviate hunger. Calorie counting, food journals, and group support through organizations such as Weight Watchers may be helpful in some motivated patients.

Pharmacologic interventions for weight loss provide adjuncts resulting in modest weight loss, but pose safety issues for dialysis patients. Orlistat, which inhibits pancreatic lipases and thereby lessens the intestinal absorption of dietary fat, is modestly effective but increases urinary oxalate excretion and has been reported to cause acute kidney injury. It therefore is best avoided in dialysis patients pending further study.

Bariatric surgery is increasingly considered as a treatment for obesity. Successful bariatric surgery generally is defined as loss of at least 50% of the weight in excess of ideal body weight and maintenance of weight loss for 5 years. Options for bariatric surgery are either restrictive (laparoscopic adjustable gastric banding and laparoscopic sleeve gastrectomy) or malabsorptive (laparoscopic Roux-en-Y gastric bypass and biliopancreatic diversion). Malabsorptive procedures result in the most dramatic weight loss, but also are associated with higher morbidity and mortality. Because of lower rates of complications, laparoscopic adjustable gastric banding is becoming more common, but dialysis patients seem to have higher rates of postoperative complications from this

procedure than the general population. Bariatric procedures are effective for weight loss in dialysis patients, with median excess body weight loss of 31%-61% reported in a review by the USRDS. Postsurgical mortality in this group of 188 patients was 3.5%, higher than in the nondialysis population undergoing bariatric procedures. Pretransplantation bariatric surgery may allow some dialysis patients to undergo successful transplantation. Such patients will need to be monitored for potential oxalate nephropathy. These patients also may require higher doses of immunosuppressives because the pharmacokinetics of medications can be altered by gastric surgical procedures.

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### Alcohol Use

There is little information about alcohol use in dialysis patients. One study of an urban hemodialysis population found that 27.6% of 164 patients scored in the alcoholism range on the Michigan Alcoholism Screening Test (MAST); the estimate in the general population is 5%-10%. The MAST is a self-reported 25-item questionnaire scored from 0-10, with scores higher than 5 indicating a high likelihood of alcoholism. In this study, male, human immunodeficiency virus (HIV)-positive, and younger (aged 55 $\pm$ 15 years) patients were more likely to score higher on the MAST screen. Being dependent on alcohol at the time of ESRD diagnosis is associated with shortened patient and transplant survival in those undergoing kidney transplantation. Screening for alcohol use is a standard part of general health care, and more information about alcohol use in dialysis patients would be helpful.

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### Tobacco Use and Cessation

Tobacco use is a modifiable cardiovascular risk factor. Smoking cessation improves general health and likely delays progressive loss of kidney function in those with CKD. Even brief repetitive advice for tobacco cessation from health care providers is effective and thus should be part of routine health care counseling in dialysis patients who smoke. Most adult smokers report wanting to stop (68.8% in a National Health Interview survey); more than half have tried quitting in the past year and 6.2% recently quit. Cessation techniques include counseling (eg, individual, group, support groups, telephone, and online) and medications (eg, nicotine patch, lozenges, gum, inhaler, spray, varenicline, and bupropion). There are no studies of cessation techniques in dialysis patients, but in the general population, 30% of successful quitters used medications, 6% used counseling, and 4.3% used both. Advice from health care professionals increases attempts to quit and the use of effective medications. These interventions can double to triple successful cessation. There are limited data about dosing medications for tobacco cessation in dialysis patients. One pharmacokinetic study of bupropion in 8 hemodialysis patients suggests that an appropriate dose for this population is 150 mg every 3 days rather than 150 mg daily as advised in nondialysis patients; bupropion does not appear to be removed by hemodialysis and metabolites accumulate. The recommended maximum daily dose of varenicline in dialysis patients is 0.5 mg.

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### Contraception and Sexual Dysfunction

#### *Overview*

Sexual dysfunction is an under-recognized, understudied, and common problem for dialysis patients. Although 30%-80% of women on dialysis therapy experience sexual dysfunction and 70% of men on dialysis therapy have erectile dysfunction, most patients do not discuss these problems with their

nephrologists, gynecologists, or primary care physicians. Having patients complete a validated survey such as the 15-item International Index of Erectile Function (IIEF) for men or the 9- or 19-item Index of Female Sexual Function Index (FSFI) for women can serve as a screen or a specific investigative tool in individual patients. Few nephrologists question dialysis patients about sexual dysfunction and many are inclined to believe primary care providers will address such issues, but it is clear that sexual dysfunction is prevalent in dialysis patients, contributes to poor quality of life, and is associated with depression. Occasionally, contraception will need to be discussed with dialysis patients, and in such instances, some basic knowledge of fertility and sexual dysfunction in dialysis patients is helpful.

Sexual dysfunction in men includes loss of libido or sexual interest, erectile dysfunction (inability to achieve or maintain an erection), problems with ejaculation, and infertility. In women, sexual dysfunction includes loss of libido or sexual interest, failure of vaginal lubrication, orgasmic impairment, vaginismus or dyspareunia, and infertility. In both men and women, normal sexual function depends on the coordination of vascular, neurologic, psychological, and hormonal systems. Abnormalities in each of these systems may occur with ESRD. Two-thirds of men on dialysis therapy have low serum testosterone levels, and most premenopausal women on dialysis therapy do not ovulate due to the lack of a pulsatile surge in luteinizing hormone. In part because sexual dysfunction in dialysis patients is poorly understood and studied, there are few validated treatment options.

### *Erectile Dysfunction*

Erectile dysfunction is the most studied aspect of sexual dysfunction in dialysis patients, yet there are few controlled studies of treatment in men on dialysis therapy. Phosphodiesterase-5 inhibitors (sildenafil, vardenafil, and tadalafil) are more effective than placebo in improving the success of sexual intercourse (69% vs 35%) and erections (67%-89% vs 27%-35%) in mixed populations of non-ESRD men with various comorbid conditions such as diabetes mellitus, hypertension, depression, stable cardiovascular disease, and radical prostatectomy for prostate cancer. There were no differences among the 3 medications in these short-term studies. The most common adverse effects were headaches, flushing, dyspepsia, back pain, and myalgia in $\leq$2%. There are few studies of these medications in patients with CKD, and safety data in this population are lacking. In the absence of contraindication, phosphodiesterase-5 inhibitors can be prescribed to men on dialysis therapy provided they are not using nitrates, which constitutes an absolute contraindication to phosphodiesterase-5 inhibitor use. There are few data about the safety and efficacy of these medications to treat sexual dysfunction in women.

Small studies suggest that oral zinc may increase testosterone levels and thus sexual function in men on dialysis therapy. Adding zinc to the dialysate does not seem to be effective. There is little information about other forms of treatment for erectile dysfunction in men on dialysis therapy.

### *Contraception*

Dialysis may be considered an effective contraceptive because most women on dialysis therapy are infertile; however, occasionally a dialysis patient may become pregnant, and repeated pregnancies in a woman on dialysis therapy have been reported. Pregnancy in women on dialysis therapy also may be becoming more common. Premenopausal women on dialysis therapy should be counseled about the possibility of pregnancy and offered contraception, especially if they continue to have regular menstrual periods. For most patients, this may be done best by the woman's gynecologist or primary care provider, but the issue should be addressed and appropriate care should be coordinated. If there is a possibility of conception, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and probably direct renin inhibitors should be avoided due to risks of fetal abnormalities. Available methods for contraception include intrauterine devices (best avoided in women on peritoneal dialysis therapy), hormonal therapies, and barrier methods. There is little information about contraceptive use in women with CKD and those treated by dialysis, but the contraindications for specific therapies in the general population typically also apply to such patients.

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## SCREENING FOR COGNITIVE IMPAIRMENT AND DEPRESSION

### Cognitive Impairment in ESRD

Cognitive impairment affects 16%-38% of dialysis patients who undergo neuropsychological testing. The prevalence depends on the definition of impairment, the sample tested, and the type and timing of the testing. However, cognitive impairment is 3 times higher in dialysis patients than in age-matched general population controls. "Mild cognitive impairment" is a term describing a level of impairment that is more than that associated with normal aging, but that does not meet the criteria for dementia. The annual rate of progression from mild cognitive impairment to dementia ranges from 5%-20%. Dementia is a chronic and progressive cognitive dysfunction featuring impaired memory and loss of function in at least one other domain of cognition, such as reasoning, orientation, attention or executive function, language, or the skills needed for planning and sequencing tasks. Dementia requires a decline from one's baseline cognitive level and must be severe enough to hinder independence and daily activities. Alzheimer dementia and vascular dementia are the most common forms of dementia in the United States. Widespread vascular disease and specifically cerebrovascular disease in dialysis patients may contribute to the high prevalence of dementia in this population. Anemia and albuminuria also are associated with dementia. Risk factors for dementia in dialysis patients mirror those in the general population and include age, nonwhite race, and female sex. Between 30% and 55% of patients with ESRD who are older than 75 years have cognitive impairment, yet 10%-30% of young or middle-aged patients with ESRD also exhibit cognitive impairment; therefore, screening based on age alone is inappropriate in this population.

Delirium is a syndrome of cognitive impairment defined as inattention and altered consciousness that occurs in the setting of a medical condition or pharmacologic therapy. Unlike dementia, delirium develops acutely, often exhibiting a fluctuating course. Dialysis patients can develop delirium in response to a variety of medications, including narcotic analgesics, tramadol, gabapentin, cyclobenzaprine, and sedative hypnotics. The development of delirium should heighten the suspicion for underlying dementia because the conditions can coexist and delirium may unmask an underlying dementia. Cognitive impairment affects and complicates the management of medical illnesses. Thus, screening for cognitive impairment in dialysis patients is worthwhile for decision making, identifying treatable causes, and potentially improving outcomes. Importantly, identifying mild cognitive impairment provides opportunities and direction for beginning advance care planning with patients and families.

**Table 3.** Dementia Screening Tests

| Instrument | Administration Time | Comments |
|---|---|---|
| Mini-Mental State Examination | 7-10 min | Norms available, does not test executive function |
| Montreal Cognitive Assessment | 10 min | Evaluates executive function |
| Clock Drawing Task | 1-3 min | Evaluates executive function, less cultural bias |
| Mini-cog | 3-4 min | Clock drawing + 3-word recall |
| KDQOL Cognitive Subscale | 1-2 min | Self-report, validated in ESRD |

*Note:* Adapted from Kurella Tamura M, Yaffe K. Dementia and cognitive impairment in ESRD: Diagnostic and therapeutic strategies. *Kidney Int.* 2010;79:14-22.

Abbreviations: ESRD, end-stage renal disease; KDQOL, Kidney Disease Quality of Life.

Multiple screening tests for dementia exist, and their use will depend on the time available, frequency required, and clinical conditions anticipated. Scores on most screening tests can be affected by age, educational level, and English fluency. Ideally, screening should begin before a patient reaches ESRD. Available screening tests that can be performed in less than 10 minutes are listed in Table 3. The Mini-Mental State Examination (MMSE) is the best known of the screening tests. A score less than 24 points (maximum is 30) has >80% sensitivity and specificity for dementia. Because the MMSE does not test executive function and deficits in executive function are prominent in vascular dementia, its use may be limited in the dialysis population. Most screening tests have high sensitivity but variable specificity. Comprehensive neuropsychological testing may be suggested in some patients. It is important to exclude delirium and depression as reversible treatable causes of cognitive impairment before diagnosing dementia.

When dementia is diagnosed, attention should be focused on associated functional impairments and needs (eg, finances, performance of daily activities, behavioral disturbances, patient safety, and advance care planning). Treatment should address any associated conditions, such as depression and sleep disturbance, and also should consider medications for dementia. Cholinesterase inhibitors (donepezil, tacrine, rivastigmine, and galantamine) and *N*-methyl D-aspartate receptor antagonists (memantine) are available for the treatment of Alzheimer dementia, and some may have efficacy in vascular dementia, although they are not approved for that indication. The

clinical benefit of these agents is modest (a 4- to 6-month delay in cognitive decline) and long-term outcome effects are unclear. There are no data for the use of these medications in patients with ESRD, so treatment must be individualized. There are limited data for the effects of dialysis adequacy (by Kt/V) or frequency and blood pressure management on dementia.

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### Depression

Depression occurs in 2%-10% of the general population, but in 20%-30% of hemodialysis patients. Depressed dialysis patients have lower quality of life, more functional impairment, increased pain, and poorer adherence to medical treatments. They also have more frequent hospitalizations and higher mortality. In addition, depression can affect cognition. Despite the high prevalence and poor outcomes associated with depression in dialysis patients, depression is diagnosed and treated in a minority of patients. Like cognitive impairment, depression can affect both the patient's and his or her family's response to treatment and engagement in advance care planning. Identifying depression in a dialysis patient therefore can affect overall care and quality of life, as well as somatic symptoms and response to dialysis therapy. Because depression affects patient outcomes and overall goals for care, screening for depression in dialysis patients is worthwhile.

Commonly used self-reported depression screening tools such as the Beck Depression Inventory, Patient Health Questionnaire, and Center for Epidemiologic Studies Depression Scale have been validated in dialysis patients. Somatic symptoms that are characteristic of depression (eg, fatigue, sleep disorders, loss of energy, decreased appetite, and trouble concentrating) may be more common in dialysis patients, but in order to diagnose depression, these somatic symptoms must be accompanied by either loss of interest (anhedonia) or feelings of sadness (depressed mood). Most depression screening tools can be completed in a few minutes and, in select patients, will be a necessary accompaniment to screening for cognitive impairment.

After depression is diagnosed, treatment should be tailored to the individual patient based on resources and needs. There are few studies of depression treatment in dialysis patients. Pharmacologic and nonpharmacologic approaches may be involved. Studies of selective serotonin reuptake inhibitors in dialysis patients have been reported, but generally include small numbers of patients in short-term studies. As in nondialysis patients, efficacy may be improved in the dialysis setting by combining cognitive behavioral therapy with pharmacologic treatment, but time, appropriate resources, patient commitment to therapy, and the limited published data for efficacy in dialysis patients may limit options (see Hedayati et al for recommendations and effects of specific medications). Additional nonpharmacologic treatments that may hold promise in the treatment of depression in dialysis patients include more frequent dialysis and exercise training programs.

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## ADVANCE CARE PLANNING

Advance care planning should be part of the periodic care plan for each dialysis patient. Contemporary advance care planning is a patient-centered process that occurs primarily between patients and their families and loved ones. Patients expect their dialysis care providers and nephrologists to prompt the discussions, and the considerations involved in advance care planning under the conditions of coverage of the Centers for Medicaid and Medicare mandate that dialysis units promote the process. For most dialysis patients, it is their quality of life that influences whether they accept or reject interventions aimed at prolonging life. Because each individual's quality of life changes over time, each patient's goals for care also will change, making advance care planning an ongoing and active process rather than a one-time discussion. The trajectory of illness characterizing ESRD is one of gradual decline in functional status punctuated by acute episodes resulting in a further loss of function from which the patient typically never completely recovers. Examples of such acute episodes are myocardial infarction, amputation, episode

of bacteremia, and often any hospitalization. These episodes, or sentinel events, are opportunities for re-addressing the goals of care and, if needed, advance directives.

Advance directives cannot anticipate all medical situations and are completed by only a third of patients. Directives may not be consulted in every setting or circumstance and therefore cannot be relied upon to direct treatments. However, some advance directives remain useful and beneficial for dialysis patients, including designation of a surrogate decision maker or health care proxy and do-not-resuscitate preferences. In states or areas where they are available, physician orders for life-sustaining treatment or the equivalent should be offered to dialysis patients. These documents are signed physician orders detailing specific interventions desired or rejected by the patient (eg, do not resuscitate, administration of intravenous fluids, antibiotics, nutrition, and dialysis). Patients and families use the advance care planning process to facilitate discussions, prepare for death, identify and educate surrogate decision makers, achieve control over medical care, relieve burdens on loved ones, strengthen relationships, clarify goals, and prepare for in-the-moment decision making that may be required. Advance care planning therefore will occur throughout the course of CKD. Ideally, such discussions will accompany considerations of renal replacement therapy at times of sentinel events, as part of the routine care plan for each patient and when issues are raised by patients and families. Some assessment of prognosis is implicit in advance care planning and required for informed decision making. Tools are available to aid the nephrologist in assessing prognosis (eg, at touchcalc.com/calculators/sq) and are based on known prognostic factors, such as patient age, comorbid conditions, serum albumin level, functional status, and the "surprise" question (answering no to the question, "Would I be surprised if this patient died within the next 6 months?"). The clinical practice guideline *Shared Decision-Making in the Appropriate Initiation of and Withdrawal From Dialysis* has valuable toolkits and recommendations to aid nephrologists in this aspect of the general care of dialysis patients.

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