End Stage Renal Disease For the Primary Care PA

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Outline

• How does dialysis work?
• Dialysis as the forerunner of bioethics
• The growing ESRD population
• Management of comorbidities
• Preventive health
Hemodialysis Illustrated

[Diagram of hemodialysis process showing blood filtration and dialysis machine connection.]

Types of Access for Dialysis

- **Fistula**: Artery → Synthetic tube → Vein
- **Graft**: Artery → Synthetic tube → Vein
- **Needles connecting to machine**: Artery → Needle connecting to machine → Vein

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Diffusion vs Convection

Hemodialysis
- Blood flows through the dialyzer
- Solute moves by diffusion across the semipermeable membrane

Hemofiltration
- Blood flows through the filter
- Fluid moves by convection caused by hydrostatic pressure difference
- Water and solutes are removed by filtration
Dialysis Access Care

- Avoid Needle Sticks or BP measurement in “access” arm.
How did it all start?

Willem Kolff (1911-2009)

Pioneer of artificial organs
Outpatient dialysis is born

Belding Scribner (1921-2003)

1st implantable shunt
“Life or Death” Committee

Lawyer, Banker, Minister, Housewife, State Official, Labor Leader, and Surgeon

The Beginning of Bioethics

• “HOUSEWIFE: If we are still looking for the men with the highest potential of service to society, then I think we must consider that the chemist and the accountant have the finest educational backgrounds of all five candidates....
• “LAWYER: Both these men have made provisions so that their deaths will not force their families to become a burden on society.
• “STATE OFFICIAL: But that would seem to be placing a penalty on the very people who have perhaps been most provident....
• “SURGEON: How do the rest of you feel about Number Three—the small businessman with three children? I am impressed that his doctor took special pains to mention that this man is active in church work. This is an indication to me of character and moral strength....
• “LAWYER: It would also help him endure a lingering death.....
• “MINISTER: Perhaps one man is more active in church work than another because he belongs to a more active church.
• “LABOR LEADER: For the children’s sake, we’ve got to reckon with the surviving parent’s opportunity to remarry, and a woman with three children has a better chance to find a new husband than a very young widow with six children.”

**Stages of CKD**

**Table 3. Chronic Kidney Disease: A Clinical Action Plan**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>Action*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>≥90 (with CKD risk factors)</td>
<td>Diagnosis and treatment, Treatment of comorbid conditions, Slowing progression, CVD risk reduction</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild ↓ GFR</td>
<td>60–89</td>
<td>Estimating progression</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30–59</td>
<td>Evaluating and treating complications</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15–29</td>
<td>Preparation for kidney replacement therapy</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 (or dialysis)</td>
<td>Replacement (if uremia present)</td>
</tr>
</tbody>
</table>

Shaded area identifies patients who have chronic kidney disease; unshaded area designates individuals who are at increased risk for developing chronic kidney disease. Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m² for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

* Includes actions from preceding stages.

**Abbreviations:** GFR, glomerular filtration rate; CKD, chronic kidney disease; CVD, cardiovascular disease
ESRD population steadily increasing

New patients: Nearly 117,000 people began treatment for end-stage renal disease (ESRD) in 2010.

Total patients: Nearly ten times more patients are now being treated for ESRD than in 1980.

USRDS Annual Report 2012
ESRD patients are living longer

People are surviving longer on dialysis than in the past.

But mortality for dialysis patients is still far higher than in the general population.

Among hemodialysis patients, the adjusted number of deaths per 1,000 patient years at risk has fallen 26% since 1985.

USRDS Annual Report 2012
ESRD care is expensive

**Costs of caring for patients with ESRD, 2010**

1.3% of Medicare patients have ESRD

- **ESRD: 410,000 patients**

They account for 7.5% of Medicare spending

- **$25.8 billion**

**TOTAL MEDICARE SPENDING**

$343 BILLION
Median survival is 3 years

Adjusted survival probabilities, from day one, in the ESRD population

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
<th>36 months</th>
<th>48 months</th>
<th>60 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>0.84</td>
<td>0.75</td>
<td>0.59</td>
<td>0.47</td>
<td>0.38</td>
<td>0.30</td>
</tr>
<tr>
<td>1999</td>
<td>0.84</td>
<td>0.74</td>
<td>0.60</td>
<td>0.48</td>
<td>0.38</td>
<td>0.31</td>
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<tr>
<td>2001</td>
<td>0.84</td>
<td>0.75</td>
<td>0.60</td>
<td>0.49</td>
<td>0.40</td>
<td>0.32</td>
</tr>
<tr>
<td>2003</td>
<td>0.84</td>
<td>0.74</td>
<td>0.61</td>
<td>0.50</td>
<td>0.40</td>
<td>0.33</td>
</tr>
<tr>
<td>2005</td>
<td>0.84</td>
<td>0.75</td>
<td>0.62</td>
<td>0.51</td>
<td>0.42</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Adjusted 60 month survival probability for transplant patients is 73%
CV Disease contributes to mortality

- Arrhythmia/cardiac arrest: 26.5%
- Infection: 10.9%
- Withdrawal: 10.5%
- Malignancy: 3.7%
- CVA: 3.3%
- Other cardiac: 1.9%
- CHF: 5.0%
- AMI: 4.9%

All other: 33.4%
CV Disease

• CV Disease is the leading cause of death
  – 22% of all deaths in ESRD pts secondary to sudden cardiac death

• CV mortality markedly greater in ESRD than general population (5-100x)

• 2 year mortality ~ 75% after AMI

• LVH, accelerated arteriosclerosis, valvular calcifications, pericarditis, autonomic dysregulation, fluid and electrolyte shifts
CV Disease Management

• ECHO at baseline and every 3 years
• EKG baseline and annually
• For contrast studies, consideration of iso-osmolar contrast and N-acetylcysteine for pts with residual renal function
• Avoid brachial or radial artery approach or IJ vein (future access for dialysis)
CV Disease Management

• Maintain “dry weight” on dialysis
• Nocturnal dosing of BP medications
• Clearance of BP drugs on dialysis
• Avoid excess fluid accumulation
  – Low salt diet 2 gm/day, fluid restriction 1.5 L/day, increased UF, longer or more frequent dialysis
• Statins lessen vascular risk, but effect is much smaller than in general population
HTN and ESRD

- 28% of new ESRD patients have HTN as principal diagnosis
- HTN(>135/85) prevalent in 82% of ESRD pts
- Thigh or leg measurement in patients who have had multiple upper extremity surgeries
- Consider clearance of HTN drugs with dialysis as well as prolonged T\(_{1/2}\) life.
Clearance of HTN drugs with dialysis

Table 10. Removal of Antihypertensive Drugs with Dialysis

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Percent Removal with Dialysis</th>
<th>HD</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACE Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benazepril</td>
<td>Yes</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Enalapril</td>
<td>35</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>50</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Ramipril</td>
<td>Yes</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td><strong>Calcium Channel Blockers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine</td>
<td>?</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>Low</td>
<td>Low</td>
<td>?</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Felodipine</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Low</td>
<td>Yes</td>
<td>?</td>
</tr>
<tr>
<td><strong>β-Blockers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atenolol</td>
<td>75</td>
<td>53</td>
<td></td>
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<tr>
<td>Alocronolol</td>
<td>70</td>
<td>50</td>
<td></td>
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<tr>
<td>Carvedilol</td>
<td>None</td>
<td>None</td>
<td>None</td>
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<tr>
<td>Labelolol</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td></td>
</tr>
<tr>
<td>Metoprolol</td>
<td>High</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td><strong>Antidiuretin Drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonidine</td>
<td>5</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Guanabenz</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Methylodopa</td>
<td>60</td>
<td>30-40</td>
<td></td>
</tr>
<tr>
<td><strong>Vasodilators</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hydralazine</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Minoxidil</td>
<td>Yes</td>
<td>Yes</td>
<td>?</td>
</tr>
<tr>
<td><strong>Angiotensin Receptor Blockers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Losartan</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Cardesartan</td>
<td>None</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Eprosartan</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Telmisartan</td>
<td>None</td>
<td>None</td>
<td>?</td>
</tr>
<tr>
<td>Valsartan</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

AJKD 2005;45(4) Supp.3:S53
## HTN Therapy in ESRD

### Table 12. Antihypertensive Drug Therapy in Dialysis: Guidelines for Selection

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Preferred</th>
<th>Relatively or Absolutely Contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina pectoris</td>
<td>β-Blockers, CCBs</td>
<td>Direct vasodilators</td>
</tr>
<tr>
<td>Post-MI</td>
<td>Non-ISA β-blockers</td>
<td>Direct vasodilators</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy with diastolic dysfunction</td>
<td>β-Blockers, diltiazem, verapamil</td>
<td>Direct vasodilators, α₁-blockers</td>
</tr>
<tr>
<td>Bradycardia, heart block, sick sinus syndrome</td>
<td></td>
<td>β-blockers, labetalol, verapamil, diltiazem</td>
</tr>
<tr>
<td>Heart failure (decreased LV ejection fraction)</td>
<td>ACE inhibitors, ARBs, β-blockers</td>
<td>CCBs</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td></td>
<td>β-blockers</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>ACE inhibitors, ARBs</td>
<td>β-blockers</td>
</tr>
<tr>
<td>Asthma/COPD</td>
<td></td>
<td>β-blockers</td>
</tr>
<tr>
<td>Cyclosporine-induced hypertension</td>
<td>CCBs, labetalol</td>
<td>Nicardipine, verapamil, diltiazem</td>
</tr>
<tr>
<td>Liver disease</td>
<td></td>
<td>Labetalol, methyldopa</td>
</tr>
<tr>
<td>Erythropoietin-induced hypertension</td>
<td>Calcium antagonists</td>
<td>ACE inhibitors</td>
</tr>
</tbody>
</table>

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*a* May increase serum levels of cyclosporine

*b* May increase erythropoietin requirement
HTN Therapy in ESRD

- Atenolol and lisinopril have prolonged $T_{1/2}$ life and may be given 3 times per week after dialysis
- CCBs pharmacokinetics are unaltered and appear more effective in volume expansion
- ARBs also have preserved pharmacokinetics
- Clonidine transdermal patch
Diabetes and ESRD

- 44% of new ESRD cases have diabetes as principal diagnosis

- Increased risk of hypoglycemia
  - Reduced degradation of insulin
  - Impaired renal gluconeogenesis
  - Target HbA1c > 7%

- HbA1c likely underestimates blood glucose levels.
  - Use in conjunction with home glucometer readings
  - Glycated albumin levels may be more accurate
Diabetic Therapy in ESRD

• Avoid 1\textsuperscript{st} generation sulfonylureas (glipizide preferred)
• Avoid metformin; risk of lactic acidosis
• Thiazolidinediones may cause fluid retention
  – Contraindicated with CHF
• DPP-4 inhibitors (i.e. gliptins) - sitagliptin ok
• Meglitinides - avoid completely
• Insulin - preferred for ESRD pts.
Anemia Management

- EPO stimulates RBC production by bone marrow
- Insufficient EPO production in ESRD
- Prior to 1990, transfusions were the norm
  - Hepatitis B, hepatitis C, HIV
  - Immune sensitization (problem for transplant)
  - Iron overload
  - Transfusion reactions
Anemia Management

• Benefits of EPO Stimulating Agents
  – decreased need for transfusions
  – Improvement of LVH
  – Improved hemodynamics
  – Improved cognition
  – Improved quality of life
Anemia Management

• However...
  – Increased risk of stroke
  – Associated with tumor progression
  – Risk of access thrombosis
  – May worsen HTN

• Use with caution in patients with a history of stroke or malignancy
Anemia Management

• Initial Hgb<10 g/dL. Target Hgb 11-12 g/dL.
• Dosage is 50-100 units/kg 3 x per week
• Hyporesponsiveness
  – Iron deficiency
  – Bone disease from secondary HPT
  – Myeloma/MDS/Myelofibrosis
  – Chronic inflammation (old transplant or AV graft)
  – Aluminum toxicity
Secondary Hyperparathyroidism

• Complex interplay between ↓calcium, ↑PO4, ↓vitamin D, and ↑FGF-23↔↑ PTH
• Renal Osteodystrophy
  – Weakness, fractures, bone and muscle pain, avascular necrosis
• Vascular calcification
  – Transformation of VSMC to osteo/chondrocytic like cells
• Vitamin D deficiency is common
  – Check 25-OH Vit D levels
Secondary Hyperparathyroidism

• Treatment
  – Ergocalciferol to target a level >30 ng/mL
  – Active Vitamin D sterols
  – Dietary PO4 restriction
  – PO4 binders (non-calcium)
  – Calcimimetic (cinacalcet)

• Targets
  – Intact PTH = 150-300 pg/mL
  – PO4 = 3.5-5.5 mg/dL
  – Ca = 8.4-9.5 mg/dL
Vaccinations

• Lower antibody titers and less sustained response to immunizations
• Helps prevent spread of infection through dialysis unit
• Techniques to help effectiveness
  – Altered scheduled
  – Increased dose
  – Adding adjuvants
  – Dual vaccination
Hepatitis B

- Responsible for outbreaks in dialysis units during the 70’s and 80’s
- 34-88% of patients develop seroprotective antibodies
- Increased dose (40 mcg) given 3-4 times
- Should be given early in the course of CKD for better response (prior to ESRD)
Influenza and H1N1

• 36-90% of patients develop seroprotective antibodies
• H1N1 mortality as high as 5% in ESRD pts
• Studies suggest only a marginal benefit to vaccination, but prone to bias
## Recommended Vaccines

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

*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.
Cancer Screening

• High mortality of ESRD pts makes routine screening inappropriate

• Utility depends on personal risk, expected survival, and transplant status

• Reported <= 5 days days of life saved per pt with routine screening
  – Least effective in ages 50-70 yrs old, women, and Caucasians
Cancer Screening

- Acquired renal cystic disease associated with renal cell carcinoma
  - However, routine screening of all pts not cost effective
- Breast and Colon cancer are not more common in ESRD population
- With exception of prostate, ESRD pts are not more likely to be given a diagnosis of late stage cancer
Cancer Screening

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.
Hearing and Vision

• Sensorineural hearing loss occurs in 46-77% of dialysis patients
• Similar physiologic processes in kidney and cochlea in transport of fluid and electrolytes
• Etiology includes electrolyte disturbances, HTN, aminoglycosides, nerve conduction dysfunction
• Periodic auditory testing is recommended
• Medicare does not cover hearing aids
Hearing and Vision

- More commonly affected by cataracts, optic neuropathy, retinopathy, macular degeneration
- Genetic disorders involve the inner retina and glomerulus
- Regular ophthalmology exams recommended, especially for diabetics.
Fall Assessment and Fractures

• Fractures occur in 10-40% of dialysis patients and in about 50% of pts older than 50 years.
• Hip fractures are 4 times more common
• Bone mineral density has limited fracture prediction in ESRD pts – not recommended in dialysis patients.
• Risks for hip fracture include age, female, white, lower BMI, lower albumin, CVD, and need for assistance with ambulation
Fall Assessment and Fractures

• Falls are more common in ESRD pts
• Risks include age, comorbidities, mean predialysis SBP, previous fall
• Procedure related risk
• Home safety evaluation, OT, PT
• Assess 25-OH Vit D levels
• Exercise training to improve muscle strength
Exercise

• Only 13% of ESRD pts get recommended level of physical activity (30 min 3x/week)
• Rarely assessed by nephrologists
• Renal Exercise Demonstration Project
  – 8 weeks home based training
  – 8 weeks cycling during hemodialysis
  – 12% increase in physical performance and HR-QOL
• Effects of exercise on inflammatory markers appears minimal
Obesity

• 30% of dialysis patients are obese
• Limited data on treatment strategies and clinical effectiveness
  – Increased BMI associated with increased survival (The Obesity Paradox)
• Obesity is barrier to transplant
• Bariatric surgery results in excess body weight loss of 31-61%