Our Common Goals

- Recent surveys noted that the three top subspecialist to maintain their internal medicine certification was Geriatrics followed by Pulmonary/Critical Care and Nephrology.
  - Highlight End of Life/Quality of Life Issues
- Arizona Kidney Disease and Hypertension Center (AKDHC) is the largest Nephrologist owned practice in the nation. It services all of Arizona and strives to set the standard of care.
- Jean Robey, MD has practiced in Sun City/Sun City West area for nearly 6 years and >80% of her practice is >65 years of age.
- Nearly half of ESRD patient > 65 years of age.
- AKDHC is embarking on studies to evaluate how to best serve/prepare our Geriatric patients with CKD Stage 4 modules and with studies to look at proper preparation for dialysis needs.

Objectives

- Discuss the Prevalence of Chronic Kidney Disease (CKD) - THE EPIDEMIC
- Discuss the methods of identifying patients with Chronic Kidney Disease
  - MDRD vs CKD EPI equation
- Review the risk factors for Chronic Kidney Disease
- Review the co morbidities that accompany Chronic Kidney Disease
- Emphasize on the multiplicity of Chronic Kidney Disease on mortality
- Discuss the effects of Anemia of Chronic Kidney Disease on patients, specifically the impact in Long Term Care settings
- Discuss the effects of Vitamin D deficiency on Chronic Kidney Disease patients
Stages of Chronic Kidney Disease

**Stages of Chronic Kidney Disease**

**Anatomical Abnormalities**
- Solitary kidney
- Kidney asymmetry
- Kidney stones
- Renal cystic disease
- Medullary Sponge Disease

**Decrease in function supported by 24hr urine collection or calculated by equations**

**Disease modification**
- Comorbid maximization
- GFR Conversion identification and treatment

---

**Stages of CKD**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR</th>
<th>Symptoms and risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or increased GFR</td>
<td>&gt;45</td>
<td>BP ++</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with risk (GFR 30-50)</td>
<td>30-50</td>
<td>BP Lab ++</td>
</tr>
<tr>
<td>3</td>
<td>Moderate fall in GFR</td>
<td>15-29</td>
<td>BP Lab +++</td>
</tr>
<tr>
<td>4</td>
<td>Severe fall in GFR</td>
<td>15-29</td>
<td>BP Lab +++</td>
</tr>
</tbody>
</table>

---

Prevalence of Chronic Kidney Disease

26 million people have CKD

Additional 20 million are at risk

- Risk factors include
  - Hypertension (27%)
  - Diabetes (44%)
  - Age
  - Race - minorities
  - Obesity
  - Coronary artery disease
  - Proteinuria of any cause

**USRD incidence of ESRD by AGE**

- Nearly half of all new ESRD patients are > 65 years of age
- More than one third are > 70 years of age
- 30 to 50% of YOUR patients may be at risk for developing ESRD

The information in this document may not be reproduced or disclosed to unauthorized parties without the prior consent of the Arizona Geriatrics Society.

© 2010 Arizona Geriatrics Society. All Rights Reserved
Methods of Evaluation

- "Laboratory Nephropathy"
- Based on 191,354,358 Creatinine tests ordered 1996 and assuming annual growth rate of 3%, serum Creatinine is ordered 281 million times annually in the United States.
- Formulation of Glomerular Filtration Rate (GFR) estimating equations
  - Creatinine assays were recently standardized
    - Crockcroft-Gault equation (1973)
      \[
      \text{Cockcroft-Gault GFR} = \frac{(\text{140-age}) \times (\text{Wt in kg}) \times (0.85 \text{ if female})}{(72 \times \text{Cr})}
      \]
    - Urinary clearance of creatinine and 100% men with no race discrepancy
    - Cannot be re-expressed for standardized serum creatinine
  - Underestimation of measured GFR at higher estimated GFR by MDRD Study equation is well known

- Methods of Evaluation
  - MDRD Study (1999)  
    \[
    \text{GFR} = 186.3 \times \text{SerumCr}^{1.154} \times \text{age}^{0.203} \times 1.212 \times \text{1.037} \times \text{1.018} \text{if female} \times \text{1.159} \text{if black}
    \]
    - No weight variable but > 5X large population of minimal racial diversity
    - 100% CKD
  - CKD-EPI (2009)  
    \[
    \text{GFR} = \frac{\text{141} \times \text{min(SerumCr/1.2) \times X max(SerumCr/0.75) \times 0.993}^{\alpha} \times 1.018^{\beta} \times 0.988^{\gamma} \times 1.037^{\delta}}{\text{body mass index}^{0.152} \times \text{age}^{0.203} \times \text{0.742 if female} \times \text{1.159 if black}}
    \]
    - No weight variable but again nearly 5X larger population of MDRD Study of increasing racial diversity
    - One quarter non-CDK

The information in this document may not be reproduced or disclosed to unauthorized parties without the prior consent of the Arizona Geriatrics Society. © 2010 Arizona Geriatrics Society. All Rights Reserved
Comparison Table of Three Leading Equations

Estimating Renal Function - GFR

Calculation of Function and Elderly

- Spruill et al 2008 Am J Geriatric Pharmacology
- "Although MDRD may be useful for estimating GFR, the Cockcroft-Gault equation should still be used for making adjustments in elderly individuals with renal insufficiency."
- Weight based
- Later, comments on estimating fall risk
Summary

- Chronic Kidney Disease can be Staged from Stage 1-5
- Prevalence of Chronic Kidney Disease is 26 million
- Nearly half of all new ESRD patients are > 65 years of age
- Appropriate identification of patients with Chronic Kidney Disease is important.
- Certain methods of estimating kidney function have inherit errors due to standardization of Creatinine assays.
- In populations where CKD may be more “normal” then use of CKD EPI calculation will be more accurate.
- In older populations MDRD est GFR may be more accurate but in general are very similar to CKD EPI calculations.

Once Identified - Prevention and Attention

CKD Risk Modification
- Hypertension
- Diabetes
- Hyperlipidemia
- Avoidance of Nephrotoxic agents
  - NSAIDs
  - Iodine contrast
  - Herbal supplements
- Weight loss
- Smoking Cessation

CKD accompany comorbid conditions
- Electrolyte disorders
- Acid-Base disturbances
  - Chemical inefficiency
  - Bone metabolism disorder
- Bone metabolism disorder
  - Cardiovascular risk
  - Bone fractures/pain/skin lesions
- Anemia
  - Cardiovascular risk
  - Quality of life
  - Falls

Effects of CKD on Mortality

All-Cause Mortality Sharply Increased With Decline in GFR

As independent, graded association was observed between a reduced estimated GFR and the rate of death, cardiovascular events, and hospitalization in a large, community-based population. These findings highlight the clinical and public health importance of early identification and treatment of CKD.

**Estimated GFR**

<table>
<thead>
<tr>
<th>Estimated GFR (mL/min/1.73m²)</th>
<th>All-cause Mortality</th>
<th>Any Cardiovascular Event</th>
<th>Any Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>15-29</td>
<td>1.3 (1.01-1.62)</td>
<td>1.4 (1.15-1.76)</td>
<td>1.3 (1.01-1.58)</td>
</tr>
<tr>
<td>30-44</td>
<td>1.63 (1.25-2.14)</td>
<td>2.1 (1.62-2.76)</td>
<td>1.5 (1.05-2.15)</td>
</tr>
<tr>
<td>45-59</td>
<td>2.0 (1.58-2.56)</td>
<td>2.4 (1.96-3.00)</td>
<td>1.7 (1.24-2.36)</td>
</tr>
<tr>
<td>60-89</td>
<td>2.4 (1.96-3.00)</td>
<td>2.9 (2.39-3.66)</td>
<td>2.1 (1.61-2.76)</td>
</tr>
</tbody>
</table>

Two Points of Interest

Paracrine function

**Anemia of Chronic Kidney Disease**
- Kidneys produce Erythropoietin (EPO) in response of hypoxia.
- EPO a cytokine for erythrocyte (red blood cell) precursors in the bone marrow.
- Erythropoietin analog or erythropoietic stimulating agents (ESA) can be given to CKD patients.

**Vitamin D production in Chronic Kidney Disease**
- Calcitriol is 1,25(OH)2 Vitamin D3, the active form of vitamin D.
- Calciferol (vitamin D3) which is synthesized in skin exposed to the ultraviolet rays of the sun.
- Calciferol is converted in the liver into 25(OH) vitamin D3.
- This is carried to the kidneys (bound to a serum globulin) where it is converted into calcitriol.
- Final steps involve parathyroid hormone (PTH)/intestinal absorption.

Anemia of Chronic Kidney Disease

Kidney is the major productive source of Erythropoietin (EPO).

Liver makes up 10% of production.

The interstitial fibroblasts and proximal tubule cells sense hypoxia and produce EPO.

Prevalence of Anemia in CKD - PAERI Study

- Evaluation of Prevalence and Occurrence of Anemia in progressively worsening CKD
  - 5222 predialysis patients with CKD
  - Hgb of < 12 mg/dL noted increasingly so as CKD worsened
    - Prevalence of Hgb < 12mg/dL was > 42% after est GFR decreased below 60%
    - Prevalence of Hgb < 12 with est GFR 15% was >75%
    - Prevalence of Hgb < 10 with est GFR < 30% was 5-30% based on Stage CKD.
Prevalence of Anemia in CKD

- Almost half of all CKD patients are Anemic with Hgb < 12 mg/dL.
- At eGFR of < 60 there was a 36% chance of Hgb > 10 < 12 mg/dL.
- At eGFR of < 30 there was up to a 30% chance of requiring erythropoietin analog.

Anemia of Chronic Kidney Disease

- Increase risk if CKD OR ANEMIA a factor MORE so than DM
- Increase risk if CKD compounded with any disease
- Increase risk if Anemia present in any situation

Tenant of Long Term Care Setting

The inability of the elderly individual to perform basic activities of daily (ADL) living affects independence.
- Lack of independence increase need for increase care and increase risk of injury.
- The most important factor in predicting the cost of NH care is independence with ADL.

Anemia in Long Term Care Setting

- Chronic Kidney Disease, Anemia, and the Association Between Chronic Kidney Disease-Related Anemia and Activities of Daily Living in Older Nursing Home Residents
- Schnelle et al. Feb 2009
- Retrospective study of
- 24 NHs in US
- Total of 2,004 residents of whom
- 45.7% had CKD with mean eGFR of 43.3 mL/min/1.73 m² (increased with age)
- Of patients with CKD, 60.5% were anemic
- Prevalence of anemia in residents with CKD (51%) was higher than without CKD (49%)

Schnelle et al. JAMDA Feb 2009: 120-126
Additonal Studies on Prevalence

- Prevalence and Severity of Chronic Kidney Disease and Anemia in the Nursing Home Population
- McClellan et al. Jan 2010
- 82 NHs in the United States
- 794 NH residents
- 50% of residents had CKD of stage 3 or worse
- 50% of the population had anemia
- Anemia was more common in patients with CKD
- Population with co morbidities increased with increasing stage of CKD
- 87% of those with Stage 4 or 5 CKD had 5 or more comorbidities

- McClellan et al. JAMDA Jan 2010 33-41
Anemia in Long Term Care Setting

- Study of Anemia in Long Term Care (SALT): Prevalence of Anemia and its relationship with the risk of falls in nursing home residents.
- Pandya et al.
- 564 sampled residents in United States
- Mean Hgb 11.9mg/dL
- 56% deemed “anemic”
- 64% males and 53% females
- In addition to female, AA race, h/o DM, h/o CA, h/o GIB, h/o inflammatory disease ; CKD was associated with anemia.

Logistic regression model for falling
24% experienced a fall

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% Lower bound</th>
<th>95% Upper bound</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia (WBC count)</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Age &gt; 65 yrs</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Sex</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Anemia (WBC count)</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Age &gt; 65 yrs</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Sex</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Logistic regression model for reoccurrent falls
16% experienced reoccurrent fall

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% Lower bound</th>
<th>95% Upper bound</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia (WBC count)</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Age &gt; 65 yrs</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Sex</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Anemia (WBC count)</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Age &gt; 65 yrs</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
<tr>
<td>Sex</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.45</td>
</tr>
</tbody>
</table>

The information in this document may not be reproduced or disclosed to unauthorized parties without the prior consent of the Arizona Geriatrics Society.
© 2010 Arizona Geriatrics Society. All Rights Reserved
Anemia in Long Term Care Setting

- Falls
  - Age 85+, psychotropic medications, anemia were associated with more than TWICE the risk of falls
  - Ten of the 138 (7%) residents that fell were hospitalized with fractures
    - All were anemia and 9 of 10 had received psychotropic medications
- Recurrent falls
  - Age 74-84 and 85+, CKD, anemia, and psychotropic medication were associated with more than TWICE the risk of falls
- Adjusted risk of falls and recurrent falls was found to CHANGE by 19% and 24% for each 1g/dL in Hgb level respectively (p =0.001)

Additional Study CKD/anemia/falls

- Dharmarajan et al. May 2010
- 323 residents, mostly female (78%) and mean age 83.4 yrs
- Prevalence of CKD all stages (1-5)
- Prevalence Anemia
- Occurrence of Falls and outcomes of Falls

  - Results included:
    - 73.1% of patients with Stage 2 or higher CKD
    - Anemia present in 3/5 of patients but EVALUATION to determine etiology NOT evident in most
    - 24% of anemic patients had Hemoglobin of < 10% (if associated CKD Stage 3 or higher, epogen analog is indicated)
    - Worsening CKD increased incident of Anemia
    - In 12 months, 454 falls in 323 patients, 1.4 falls per patient (higher than ave)
    - 25% of falls caused injury
    - 2.4% serious enough to require hospitalization

Anemia/CKD/Falls and Calculations

- Dharmarajan et al.
- Abstract of a Retrospective study
- 1535 patients hospitalized for acute illness
- Excluded Stage 5 (< 15ml/min/1.73 m2)
- Using Cockcroft-Gault formula logistic regression analysis determined patients with CKD Stage 2-4 were 1.5 fold more likely to fall than CKD Stage 1. Hispanics were 48% less likely to fall.
- Using MDRD formula renal function and race no longer linked to falls
- Both equations showed similar (18% and 20%, respectively) decrease risk in fall for every 1 unit increase in Hemoglobin level

  - Conclusion:
    - Declining renal function in older adults increase risk of falls
    - Anemia and CKD can co-exist but are independent risk factors
    - The Cockcroft-Gault formula better identifies risk than the MDRD formula suggesting that body weight and not race influences the relationship to falls
    - Improvement in Hemoglobin can decrease risk of falls in patients with CKD

The information in this document may not be reproduced or disclosed to unauthorized parties without the prior consent of the Arizona Geriatrics Society.
© 2010 Arizona Geriatrics Society. All Rights Reserved
Summary

- Anemia is highly prevalent in Chronic Kidney Disease starting at Stage 2-3
- Anemia is a mortality multiplier
- TENANT of Care: Reduction of co morbidities that contribute to decrease level of independence preserves quality of life and reduces cost
- It is excepted that at least 50% of NH patients have CKD
- Although many reasons for falls, Chronic Kidney Disease and Anemia are highly prevalent in the elderly population and represent independent risk factors for falls and reoccurent falls
- Identifying the cause of Anemia is important
- Correcting Anemia with appropriate use of ESA if associated with CKD can improve fall risk by up to
- The utility of Cockcraft-Gault formula for predicting fall risk is compelling

Vitamin D Deficiency

- Impaired kidney function results in deficiency in 1-α hydroxylase enzyme
- Intentional decreased consumption of vitamin D containing foods
- Environmental
- Other

Vitamin D Deficiency

Overall Population
- Vitamin D deficiency is associated with cardiovascular disease, osteoporosis, poor muscle strength, falls, fractures and mortality
- Responsible treatment of vitamin D deficiency in older patients may improve neuromuscular function and alter risk of falls thus hospitalizations

CKD population
- Is Vitamin D deficiency more likely to be seen in CKD patients with proteinuria?
- Is there an association between 25-hydroxyvitamin D and somatic muscle weakness and falls in CKD pts?ESRD pts?
- Can improving vitamin D levels improve ESA usage for CKD patients?
Vitamin D deficiency and Proteinuria

- Proteinuria alone may contribute to disease progression.
- Mechanisms include mesangial toxicity, tubular overload and hyperplasia, toxicity from specific filtered compounds such as transferrin/iron and albumin-bound fatty acids, and induction of proinflammatory molecules.

Abstract Only

- Study of Early Evaluation of Kidney Disease
- Abstract
- Multicenter CKD cohort
- 1847 participants
- 387 randomly selected
- Vitamin D 25
- Vitamin D 1, 25
- Albuminuria
- Conclusion
  - Low 25D and 1, 25 D were independently associated with albuminuria
  - IL-6 may be an important intermediary

Association of 25-hydroxyvitamin D Somatic muscle weakness and Falls in End Stage Renal Disease Patients

- Association between 25-hydroxyvitamin D, somatic muscle weakness and falls risk in End Stage Renal Disease
- Boudvill et al
- Cross sectional analysis of 25 CKD-5 patients
- Falls risk assessed by quadriceps muscle strength, FallsScreen test, Berg Balance Scale, time "up and go" test, Modified Barthel Index and Falls Efficacy Scale
- Mean age 69.8 with median time on dialysis was 3.1 years
- Conclusion:
  - Suboptimal levels of 25OHD in CKD-5 are associated with reduced quadriceps muscle strength and increased falls risk
Correction of Vitamin D deficiency on Anemia Management for CKD

- Lac et al
- Retrospective cohort study of non dialysis patients with CKD all stages
- 153 patients
- Conclusion
  - Low to normal vitamin D group showed a significant dose reduction in ESA of 24% (1415 units p = 0.025)
  - Normal to low vitamin D group showed a significant dose increase in ESA but was non significant.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Serum vitamin D (ng/mL)</th>
<th>ESA dose (units)</th>
<th>ESA change (units)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low vitamin D</td>
<td>59</td>
<td>17.3</td>
<td>51.5</td>
<td>357.0</td>
<td>0.004</td>
</tr>
<tr>
<td>Normal vitamin D</td>
<td>27</td>
<td>18.0</td>
<td>33.5</td>
<td>1,010</td>
<td>0.02</td>
</tr>
<tr>
<td>Normal vitamin D</td>
<td>38</td>
<td>43.9</td>
<td>69.0</td>
<td>3,364</td>
<td>0.04</td>
</tr>
<tr>
<td>Low vitamin D</td>
<td>28</td>
<td>51.8</td>
<td>87.9</td>
<td>1,270</td>
<td>0.26</td>
</tr>
</tbody>
</table>

The average ESA dose change and change in Hb level for each group is shown along with the mean vitamin D levels. The low vitamin D group had a statistically significant change in ESA dose using paired t-test.
Summary

- Vitamin D 25 is cheap and min to low risk profile
- Vitamin D deficiency in CKD patients is associated with increase albuminuria
  - Cause or association?
- Vitamin D deficiency in ESRD patients is associated with decreased somatic muscle strength and increased fall risk
- Low vitamin D levels carry a higher need for ESA in Chronic Kidney Disease patients.

Overall Summary

- CKD is highly prevalent
- Identifying patients with the intention to reverse disease/prevent worsening/address co-morbidities is important
- Calculation of estimated kidney function has limitations but can guide recommendations/interventions
- Anemia is a risk multiplier and noted in elderly patients with and without CKD and is independently associated with increased risk of falls
- Correction of Anemia in CKD can help improve fall risk
- Vitamin D deficiency is associated with increased fall risk
- Vitamin D deficiency is associated with potentially increased ESA need
- Correction of vitamin D 25 deficiency is cheap and additional benefits are undergoing investigation

Mortality incidence for ESRD

**End Stage Renal Disease**
- First months (1-4th) – Up to 50% mortality
- First year – Up to 30% mortality
- Five year – Up to 30% mortality

**Cancer**
- Five year survival of Stage IV Colon Ca – Up to 30% mortality
Coordinating Care Paradigm

Figure 1: Model of coordinated care by CKD stage. RRT: renal replacement therapy; CKD, chronic kidney disease; Mgt. management; PCP, primary care physician; IM, internal medicine.

ESRD Success Stories

• Living on Dialysis for 5 years

CKD Stage 3-5 Video

• www.akdhc.com
  – Click on Education
  – Four videos are available to your patients
  – If you desire a CD to play in your office
    • Contact AKDHC Administration IT department
      – (602-997-0484)
    • Or jrobey@akdhc.com