**Objectives**

- Definition of CKD and Stage
- Epidemiology
- Slowing down progression of CKD
- Complications of CKD

**CKD Definition**

Criteria:

1. Kidney damage for ≥3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either:
   - Pathological abnormalities; or
   - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR <60 mL/min/1.73 m² for ≥3 months, with or without kidney damage

**COA Classification**

**Cause**
- DM, HTN, Glomerular, Tubulointerstitial, Cystic, Infectious, Stones, Obstruction, Drugs

**GFR**
- Stages 1-5

**Albuminuria**
- A1 - A3
## New KDIGO 2012 Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR</th>
<th>Definition</th>
<th>Goals of Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;90</td>
<td>Normal-High</td>
<td>Dx &amp; Treat Underlying Disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CKD/CVD Risk Reduction</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td>Mild Decrease</td>
<td>Treat Underlying Disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Slow Progressation</td>
</tr>
<tr>
<td>3a</td>
<td>45-59</td>
<td>Mild-Moderate</td>
<td>Diagnosis, Slow Progression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Monitor for Complications</td>
</tr>
<tr>
<td>3b</td>
<td>30-44</td>
<td>Moderate-Severe</td>
<td>Monitor for Complications: Anemia, HPTH, Acidosis</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>Severe</td>
<td>Slow Progression, Complications</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>Kidney Failure</td>
<td>Monitor for Uremic Complications</td>
</tr>
</tbody>
</table>

## CKD Prevalence by MDRD EGFR

<table>
<thead>
<tr>
<th>Percent of Participants in NHANES 1999-2006, USRDS 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stages 4 and 5:</td>
</tr>
<tr>
<td>Stages 3:</td>
</tr>
<tr>
<td>Stages 2:</td>
</tr>
<tr>
<td>Stages 1:</td>
</tr>
<tr>
<td>Total: 15.6% of participants had CKD</td>
</tr>
<tr>
<td>&gt;20 million Americans with CKD</td>
</tr>
</tbody>
</table>

## Epidemiology: NHANES Participants 2005-2010

Population at Risk: Older Age, Low Socioeconomic, African American, 30-40% Diabetics with CKD, 20% HTN with CKD, 9% of CVD with CKD

## Expected Remaining Lifetimes (Years) for US Population

<table>
<thead>
<tr>
<th>General U.S. population, 2004</th>
<th>ESRD patients, 2006</th>
<th>White</th>
<th>African American</th>
<th>Hispanic</th>
<th>Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>15-19</td>
<td>16.6</td>
<td>15.9</td>
<td>16.8</td>
<td>16.1</td>
<td>16.9</td>
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<tr>
<td>20-24</td>
<td>15.8</td>
<td>15.2</td>
<td>16.0</td>
<td>15.3</td>
<td>16.2</td>
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<tr>
<td>25-29</td>
<td>15.3</td>
<td>14.7</td>
<td>15.5</td>
<td>14.8</td>
<td>16.2</td>
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<tr>
<td>30-34</td>
<td>14.8</td>
<td>14.2</td>
<td>15.1</td>
<td>14.4</td>
<td>15.7</td>
</tr>
<tr>
<td>35-39</td>
<td>14.2</td>
<td>13.7</td>
<td>14.5</td>
<td>13.8</td>
<td>15.4</td>
</tr>
<tr>
<td>40-44</td>
<td>13.5</td>
<td>13.0</td>
<td>13.8</td>
<td>13.1</td>
<td>14.6</td>
</tr>
<tr>
<td>45-49</td>
<td>12.9</td>
<td>12.4</td>
<td>13.2</td>
<td>12.6</td>
<td>14.1</td>
</tr>
<tr>
<td>50-54</td>
<td>12.2</td>
<td>11.7</td>
<td>12.5</td>
<td>11.9</td>
<td>13.4</td>
</tr>
<tr>
<td>55-59</td>
<td>11.5</td>
<td>11.0</td>
<td>11.8</td>
<td>11.3</td>
<td>12.7</td>
</tr>
<tr>
<td>60-64</td>
<td>10.8</td>
<td>10.3</td>
<td>11.1</td>
<td>10.5</td>
<td>12.0</td>
</tr>
<tr>
<td>65-69</td>
<td>10.0</td>
<td>9.5</td>
<td>10.3</td>
<td>9.8</td>
<td>11.7</td>
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<tr>
<td>70-74</td>
<td>9.3</td>
<td>8.8</td>
<td>9.6</td>
<td>9.1</td>
<td>10.9</td>
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<tr>
<td>75-79</td>
<td>8.5</td>
<td>8.0</td>
<td>8.8</td>
<td>8.3</td>
<td>10.1</td>
</tr>
<tr>
<td>80-84</td>
<td>7.8</td>
<td>7.3</td>
<td>8.1</td>
<td>7.6</td>
<td>9.4</td>
</tr>
<tr>
<td>85+</td>
<td>5.0</td>
<td>4.5</td>
<td>5.3</td>
<td>4.8</td>
<td>6.9</td>
</tr>
</tbody>
</table>

U.S. data calculated from Table 2.1 in the United States life tables, Arias E. Available at https://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_09.pdf. ESRD data: prevalent dialysis & transplant patients, 2006. Expected remaining lifetimes by race & gender can be found in Reference Table H.31. Weight used to calculate overall combined-age remaining lifetimes.
Average CKD Progression: ~5 ml/min/year decline

Major determinates: Cause & Proteinuria

DM, GN, PKD >> HTN, Tubulointerstitial Disease

Estimate & Assess individual rate of GFR decline

Predict time to ESRD!

Table 112: Years Until Kidney Failure (GFR <15 ml/min/1.73 m²) Based on Level of GFR and Rate of GFR Decline

<table>
<thead>
<tr>
<th>Level of GFR Decline (ml/min)</th>
<th>10</th>
<th>6</th>
<th>4</th>
<th>2</th>
<th>10 Yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>12</td>
<td>18</td>
<td>24</td>
<td>30</td>
<td>36</td>
</tr>
<tr>
<td>1.0</td>
<td>9</td>
<td>14</td>
<td>20</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>1.5</td>
<td>6</td>
<td>11</td>
<td>16</td>
<td>21</td>
<td>25</td>
</tr>
<tr>
<td>2.0</td>
<td>3</td>
<td>7</td>
<td>12</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>2.5</td>
<td>0</td>
<td>2</td>
<td>6</td>
<td>9</td>
<td>12</td>
</tr>
</tbody>
</table>

* Average age-related GFR decline after age 39-50 years
**AKI? REVERSIBLE PROCESS**

<table>
<thead>
<tr>
<th>AKI? REVERSIBLE PROCESS</th>
<th>SLOW DOWN PROGRESSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dehydration, Overdiuresis</td>
<td>HTN: BP control</td>
</tr>
<tr>
<td>NASIDs</td>
<td>DM: Glycemic Control</td>
</tr>
<tr>
<td>Hemodynamic: BP control and Changes</td>
<td>Proteinuria/Albuminuria: ACE/ARB</td>
</tr>
<tr>
<td>Urinary Obstruction</td>
<td>Keep HCO3 &gt;22</td>
</tr>
<tr>
<td>Contrast</td>
<td>Others: Statins, Endothelin, Uric Acid, Pentoxyfyline</td>
</tr>
<tr>
<td>UTI</td>
<td>Manage CKD MBD &amp; Anemia</td>
</tr>
<tr>
<td>Medications</td>
<td>Lifestyle: Diet, Smoking Cessation, Exercise</td>
</tr>
</tbody>
</table>

**BLOOD PRESSURE GUIDELINES IN CKD: JNC 8**

- Adults ≥18 yo with CKD, Rx to lower BP at SBP ≥140 or DBP ≥90 mm Hg to goal SBP <140 and DBP <90 mmHg. (Expert Opinion - Grade E)

  Note KDIGO Guidelines: CKD and ACR >30 mg/g: Goal SBP <130/80 mmHg

- Adults ≥18 yo with DM, Rx to lower BP at SBP ≥140 or DBP ≥90 mm Hg to goal SBP <140 and DBP <90 mmHg. (Expert Opinion - Grade E)


**BLOOD PRESSURE GuideLINES in CKD: JNC 8**

- All ≥18 y/o with CKD: Rx should include an ACEI or ARB to improve kidney outcomes. (Moderate Recommendation - Grade B)

- General nonblack population (including DM) initial Rx should include a thiazide-type diuretic, CCB, ACEI, or ARB. (Moderate Recommendation - Grade B)

- General black population (including DM) initial Rx should include a thiazide-type diuretic or CCB. (For general black population: Moderate Recommendation - Grade B; for black patients with DM: Grade C)


**RAAS INHIBITION**

- Blood pressure lowering
- Antifibrotic, antiproliferative
- Renoprotection for both DM and non-DM related CKD
- Reduction in albuminuria:
  - Inflammatory response: monocyte chemotactic agent-1, RANTES
  - Vasconstriction: endothelin
  - Fibrosis: TGF-β, collagen deposition
DOUBLE RAAS INHIBITION:
COMBINATION ACE-I + ARB USE

- ON TARGET Trial: patients with CV disease
- Nephron VA-D Trial: DM + CKD stage 2-3

Blood Pressure and Albuminuria both decreased!

**HOWEVER**
- No improved cardiovascular protection
- Increased Hyperkalemia
- Increased AKI

**Bottom Line:** Dual ACEI + ARB is not recommended, but exceptions possible

RAAS MANAGEMENT IN
NONHYPERTENSIVE CKD PATIENTS

**Diabetic CKD patients:**
ACEI/ARB if ACR >30 mg/g (microalbuminuria)

**Non-Diabetic CKD patients:**
ACEI/ARB if ACR >300 mg/g (macroalbuminuria)

RAAS INHIBITION:
FUTURE DIRECTION

- Mineralocorticoid receptor antagonists (MRA):
  - Spironolactone decreases proteinuria/albuminuria in CKD patients
  - Problem: hyperkalemia!

- Future Solutions:
  - New intestinal potassium binders: patiromer (Veltassa™)
  - Search for newer MRAs with lower K+ effect

CKD AND STATIN THERAPY

- CV protection in CKD:
  - Effects on vascular stiffening
  - Endothelial cell function

- Possible renoprotective effects:
  - ↓ Proteinuria ↓ Progression
    - Increased intraglomerular pressure with dyslipidemia
    - LDL receptors on mesangial cells leading to proliferation
    - Direct effect of statins on mesangial cell proliferation
**Bottom Line:**
- CKD patients are at higher risk for CV Disease
- Statins reduce Cardiovascular Events
- Statins have an acceptable safety profile in CKD
- Statin may have some renoprotective benefits, but insufficient evidence

**Methyl xanthine derivative that acts in vivo as a phosphodiesterase inhibitor**
- Potential Benefits:
  - Antiinflammatory
  - Antiproliferative
  - Antifibrotic

**Meta-analysis 2008:**
Ten RCTs (n=476, range 14 to 127)
- Pentox reduces albuminuria by 300 mg/d
- Does albuminuria translate to better renal outcome? → PREDIAN trial

**Design:**
- Open-label, prospective, randomized
- Would adding PTF to RAS blockade slow progression in DM2 + CKD 3-4?
- PTF (1200 mg/d) (n=82) vs. control (n=87) x 2 yrs.
  - All received similar doses of RAS inhibitors

**Results:**
- eGFR: decreased by 2.1±0.4 in PTF vs. 6.5±0.4 ml/min/1.73 m² in control (p<0.001)
- Albuminuria: ~14.9% in PTF vs. +5.7% in control (p<0.001)

PTF + RAS inhibitors → decreases eGFR decline and reduction of albuminuria

**Uric Acid: Mechanisms of Disease**

**PTF + RAS inhibitors → decreases eGFR decline and reduction of albuminuria**

- RAS activation
- Oxidative stress
- Mitochondrial dysfunction
- Epithelial-mesenchymal transition
- Endothelial dysfunction
- VSMC proliferation
- Others

- Arteriolosclerosis
- Glomerular HTN
- Glomerulosclerosis
- Interstitial disease
- AKI
- Raising UA in rats can induce glomerular HTN and kidney injury without renal UA precipitation
- Metabolic syndrome
- Non-alcoholic fatty liver disease
- HTN
- DM

**Clinical Impact of Uric Acid Lowering Therapy**

Pilot studies suggest that lowering plasma uric acid (UA) < 7 mg/dL may slow progression of kidney disease in patients with CKD.

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analysis</td>
<td>Total n=753, 11 papers</td>
<td>Uric acid lowering is associated with significant lowering of serum Cr and increase of eGFR.</td>
</tr>
<tr>
<td>J-HEALTH:</td>
<td>n=7429</td>
<td>Change in serum UA inversely correlated with change in eGFR and associated with lower CV events</td>
</tr>
<tr>
<td>Japanese HTN:</td>
<td>Hypertensive patients</td>
<td></td>
</tr>
</tbody>
</table>

**URIC ACID: BOTTOM LINE**

- Large clinical trials still needed

**KDIGO 2012:**

"There is insufficient evidence to support or refute the use of UA lowering agents in CKD and either symptomatic or asymptomatic hyperuricemia in order to delay progression of CKD."

- Treatment of hyperuricemia “not benign”
  - Stevens Johnson therapy with allopurinol therapy
  - Both allopurinol and febuxostat (xanthine oxidase inhibitors) can increase urinary xanthine levels which can be nephrotoxic

**CKD & Glycemic Control**

- Intensive glycemic control to reduce CKD progression and proteinuria

  - ADVANCE, ACCORD, VADT
  - DCCT, EDIC, UKPDS

- Target HgA1C ~ 7.0

- Target HgA1C > 7% if comorbidities, limited life expectancy or risk of hypoglycemia

**Glycemic Control: Newer Agents and Renoprotective Benefits**

- Glucagon-like peptide-1 (GLP-1)
- Dipeptidylpeptidase (DPP4) inhibitors
- Sodium-glucose transport (SGLT-2) inhibitors
Dipeptidylpeptidase (DPP4) breaks down GLP-1

- **Sitagliptin**
  - Decreases albuminuria by 20% in a prospective observation study

- **Linagliptin**
  - Mainly metabolized & eliminated by liver
  - Meta-analysis of 13 RCTs involving 5500 pts: 16% reduction in a composite renal end point consisting of micro- and macro-albuminuria, loss of eGFR>50% from baseline, AKI, or death
Average American diet:
70-100 meq/day H⁺ production

Chronic Metabolic Acidosis:
- Oxidation of branched chain amino acids
- Protein degradation
- Albumin synthesis
- Impaired vitamin D synthesis & bone metabolism
- Accelerate progression of renal disease in pre-ESRD

Keeping HCO₃ >22 meq/L shown to decrease rate of eGFR decline
Average CKD dose 30-60 meq HCO₃/day

Endothelin Antagonists
- Endothelin 1 mediates secretion of pro-inflammatory cytokines, growth factors, TGF-b
  - Type A receptor (ET₁R): vasoconstriction, Na retention, podocyte dysfunction
  - Type B receptor (ET₂R): vasodilatation, Na excretion
- Avosentan (nonselective ET-1 inhibitor) was associated with increased CHF
- Clinical studies on ET₁R-selective antagonism encouraging. (RADAR trial, DKD, Phase III)

CKD & Protein Intake
- Monitor nutritional state in CKD 4-5 q3 months:
  - Albumin, Pre-albumin, Transferrin, Edema-free Weight
- Avoid high protein diet of >1.3gm/kg/day
  - CKD 3b-5 Daily Protein: 0.8gm/kg/day
  - Nephrotic Syndrome 1gm/kg/day

CKD & Salt Intake
- Effects of high Na intake:
  - Increased BP
  - Increased proteinuria
  - Glomerular hyperfiltration
  - Blunts response to RAAS blockade
- Potential 10% reduction of proteinuria due to decreased urinary Na (and not BP effect)
- Refer CKD patients for nutrition consultation
  - Na intake <2gm/day (< 90mmol)
LVH, Male, Dyslipidemia, HTN, DM, Smoking, Insulin resistance, Sedentary lifestyle.

Carbamylation of proteins, Endothelial dysfunction, Sympathetic activation, Inflammation, Oxidative stress, Wasting.

Anemia, PO4 retention, HyperPTH, Vascular calcification, Uremic toxins, Hyperhomocysteinemia, Volume overload.

Figure 1. Adjusted effect of UAC on hazard function. Solid line shows estimated relation when logit function is modeled as linear function of logUAC. Dotted lines are 80% confidence bands for more general functional relation, as estimated by P-splines. Hatchet area represents upper and lower limit of current definition of microalbuminuria (30 to 200 mg/L).
**ALBUMINURIA REDUCTION**

- BP Control
- ACEI/ARB
- DPP4-inhibitors (sitagliptin, linagliptin)
- SGLT2 inhibitors
- Pentoxifylline
- Statins
- Diet

**PREVALENCE OF ANEMIA IN CKD**

- Incidence of Anemia increases as GFR decreases
- Diabetics develop anemia at earlier stages of CKD

**PATHOPHYSIOLOGY OF ANEMIA OF CKD**

- Inflammation
  - Hepcidin
  - Macrophage Iron Sequestration
- Iron deficiency
  - Occult GI Loss
  - ↓ Fe Absorption
- Erythropoetin
  - Secondary Hyperparathyroidism

**ANEMIA OF CKD**

- EXCLUDE CAUSES OTHER THAN CKD
- REPLETE IRON STORES
  - GOAL TSAT >30%
- START ESA DOSE & TITRATE MONTHLY UNTIL HGB 10-11 GM/DL

- Testing: CBC with diff, Reticulocyte Count, Ferritin, TSAT, B12, Folate
  - No need to check Epo levels
- Frequency of testing:
  - CKD stage 3+ annually
  - On treatment: monthly → q3 months

KDOQI guidelines, 2012
Levin A et al. Study to evaluate early kidney disease. Kidney Int. 2007

Osteitis Fibrosa Cystica

Adynamic Bone Disease
Osteomalacia

Testing: Ca, PO₄, intact PTH
CKD3b yearly & CKD4-5 q3 months

- Dietary Phosphorus restriction <1000 mg/day
- Phosphorus Binders: goal PO₄ 3.5-5.5 mg/dl
  - Calcium Based: calcium acetate (PhosLo™), TUMS™
  - Non-Ca Based: Sevelamer (Renagel, Renvela™), Lanthanum carbonate (Fosrenol™)
- Goal Ca 8.5-9.5 mg/dl and Ca*Phos <55
- Vitamin D 25OH >30 ng/ml
  - Ergocalciferol 50,000 units x 6 months
- Goal PTH <110 pg/ml in CKD 3-5ND
  - Vitamin D 1,25 OH: Calcitriol, Doxercalciferol (Hectorol™), Paricalcitol (Zemplar™)
  - Calcimimetics: Cinacalcet (Sensipar™)
**Avoid NSAIDs**

**Dose Adjust Medications:**
- Metformin: GFR 30-45 review use, GFR <30 stop
- Sulfonylureas: hypoglycemia glyburide >> glipizide
- Gabapentin
- Bisphosphonates: avoid if GFR <35 ml/min
- Anticoagulation: avoid LMWH GFR <30 ml/min
- Lithium
- Review herbal remedies: e.g. avoid aristocholic acid
- Vitamins: GFR <30 ml/min renal MVI preparations (avoid excessive fat soluble vitamins)

**CKD & AKI, Hold:**
- ACE/ARB
- Review meds: Diuretics, Metformin, Digoxin, Lithium

**Intravenous Access:**
- save veins if GFR <30 ml/min
- Blood draws and IV access in dorsum of hand
- Avoid PICC lines: rotating IV’s or central access

**Bowel Prep:**
- risk of Acute Phosphate Nephropathy
- Do not use oral phosphate containing bowel preparations with GFR <60 ml/min

**CT:**
- increased risk of Contrast Induced Nephropathy with GFR <60 ml/min, dose of contrast, age >70, DM, Gout, CHF, Dehydration
- Hydration: NS 100 cc/hr 6-12 hours pre & post
- Occurs 48-72 hours after procedure

**MRI:**
- risk of Necrotizing Systemic Fibrosis (NSF) with gadolinium based contrast
- Avoid if GFR <30 ml/min

**Physical activity** to improve cardiovascular health:
- 30 minutes ≥ 5 times per week

**Achieve a healthy weight**
- BMI 20-25

**Stop smoking**

**Health Maintenance:**
- Flu vaccine yearly
- Pneumococcal Vaccination: PCV13 → PPSV23
- Hepatitis B vaccine CKD 4-5

**Definition of CKD:**
- Dx: presence or kidney damage or eGFR <60 ml/min for >3 months
- Cause of CKD, Albuminuria, Stage

**SLOW DOWN PROGRESSION** | **MANAGE COMPLICATIONS**
--- | ---
Monitor Rate of Decline | Cardiovascular Disease
Blood Pressure / RAAS Inhibition | Anemia of CKD
Glycemic Control | CKD- MBD
Albuminuria Reduction | Malnutrition
Keep HCO3 >22 mEq/L | Risk of Infection
Others: Statins, Pentoxifylline | Medications
Lifestyle: Diet, Smoking Cessation, Exercise, Immunizations
<table>
<thead>
<tr>
<th>Class</th>
<th>Drugs</th>
<th>Dosing Recommendations CKD</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihypertensives</td>
<td>RAAS inhibitors</td>
<td>Avoid in patients with suspected functional renal artery stenosis</td>
<td>Assess GFR and monitor serum K within 2 weeks of starting or after dose escalation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Temporarily suspend during AKI, planned IV contrast, bowel preparation prior to colonoscopy or major surgery</td>
<td>Do not routinely discontinue in people with GFR &lt;30 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May need dose reduction, monitor plasma levels</td>
<td>Reduce dose by 50% in people with GFR &lt;30 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For CKD Stage 5 on dialysis, carvedilol and labetalol preferred since nondialyzable</td>
<td>May need dose reduction, monitor plasma levels</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk of crystalluria when GFR &lt;15 ml/min/1.73 m2 with high doses</td>
<td>Risk of crystalluria when GFR &lt;15 ml/min/1.73 m2 with high dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neurotoxicity with benzylpenicillin when GFR &lt;15 ml/min/1.73 m2 with high dose</td>
<td>Neurotoxicity with benzylpenicillin when GFR &lt;15 ml/min/1.73 m2 with high dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor serum levels (trough and peak)</td>
<td>Monitor serum levels (trough and peak)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduce dose by 50% when GFR &lt;60 ml/min/1.73 m2</td>
<td>Reduce dose by 50% when GFR &lt;60 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluorinated quinolones</td>
<td>Reduce dose by 50% when GFR &lt;60 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aminoglycosides</td>
<td>Reduce dose by 75% when GFR &lt;30 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Quinolones</td>
<td>Reduce dose by 50% when GFR &lt;15 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td>Betablockers</td>
<td>Carvedilol</td>
<td>Avoid amphotericin unless no alternative when GFR &lt;60 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No increase in toxicity for most statins with GFR &lt;30 ml/min/1.73 m2 or on dialysis if initiated prior to dialysis, initiate with caution in patients already on dialysis</td>
<td>No increase in toxicity for most statins with GFR &lt;30 ml/min/1.73 m2 or on dialysis if initiated prior to dialysis, initiate with caution in patients already on dialysis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class</th>
<th>Drugs</th>
<th>Dosing Recommendations CKD</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antineoplastic</td>
<td>Anthracyclines</td>
<td>Have the dose when GFR &lt;30 ml/min/1.73 m2</td>
<td>Consider switch to conventional in those at high risk for bleeding</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Heparins</td>
<td>Increased risk of bleeding when GFR &lt;30 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Warfarin</td>
<td>Use lower doses and monitor closely when GFR &lt;30 ml/min/1.73 m2</td>
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<tr>
<td></td>
<td></td>
<td>NSAIDs</td>
<td>Avoid in people with GFR &lt;60 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioids</td>
<td>Avoid in people taking RAAS blocking agents or Lithium kaoferin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chemotherapeutic agents</td>
<td>Do not use if GFR &lt;30 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cytoplatin</td>
<td>Reduce dose if GFR &lt;30 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Melphalan</td>
<td>Reduce dose if GFR &lt;30 ml/min/1.73 m2</td>
</tr>
<tr>
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<td>Heparins</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Nitrogen mustard</td>
<td>Reduce dose if GFR &lt;30 ml/min/1.73 m2</td>
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<tr>
<td></td>
<td>Lithium</td>
<td>Sodium valproate</td>
<td>Reduce dose if GFR &lt;30 ml/min/1.73 m2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diamox</td>
<td>Reduce dose if GFR &lt;30 ml/min/1.73 m2</td>
</tr>
</tbody>
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