The Kidney in Aging
The changes that occur in the kidney with aging is of the most dramatic of any organ system.
Age related changes in kidney structure and function

- At age 2 GFR at adult level. Remains at 140 ml/min/1.73 msq until age 40
- Then declines by on average 8 ml/min/msq per decade
This age related decline is accelerated by:

1. Systemic hypertension
2. Diabetes
3. Lead exposure
4. Smoking
5. Atherosclerotic vascular disease
6. Male gender
Important!

- The reduction in creatinine clearance is accompanied by reduced daily urinary creatinine excretion due to reduced muscle mass.
- That means the relationship between s-creat and CrCl changes.
- S-Creat remains stable but GFR declines.
- That means your GFR can be significantly reduced but the s-creat remains normal.
eGFR

- Cockcroft-Gault formula takes age into consideration
- MDRD formula was validated in subjects between 18-70 years.
- Best method in elderly still controversial
Proteinuria

- Microalbuminuria and overt proteinuria increases with advanced age in absence of diabetes, hypertension or elevated sCr.
Renal blood flow declines by 10% per decade after age 40.

- Most profound in renal cortex.
- Redistribution from cortex to medulla.
Renal mass

- Renal mass increase from 50g at birth, to 400g at age 40.
- Then declines to < 300g at age 90
- This correlates with the reduction in BSA
- This loss in mass is cortical and medulla is mostly spared
Glomerular number decrease
Size change controversial
Shape changes with decreased lobulation
GBM undergoes folding and thickening, then condenses into hyaline material with glomerular tuft collapse
Degeneration of cortical glomeruli results in atrophy of efferent and afferent arterioles with global sclerosis.

In JXM, glomerular tuft sclerosis leads to formation of direct channels between afferent and efferent arterioles - aglomerular arterioles.
Sclerosed glomeruli

- Increases with age but at variable rate
- < 5% age 40, up to 30% age 80
<table>
<thead>
<tr>
<th>Reasons for reduction in GFR:</th>
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<tbody>
<tr>
<td>1. Reduced glomerular lobulation - reduce surface area for filtration</td>
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<td>2. Increased glomerular sclerosis - also reduce surface area</td>
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<td>3. Increase in Tubulointerstitial fibrosis</td>
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<td>4. CVS hemodynamic changes: hpt. Reduced cardiac output</td>
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<td>5. Increased cellular oxidative stress cause ET cell dysfunction</td>
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</tbody>
</table>
Age related alterations in fluid and electrolyte homeostasis

- No age-specific changes
- Aged however more prone to disturbed urea and creatinine and electrolyte abnormalities when ill
- Aged kidney can maintain normal levels in health but fail to compensate during illness.
Disorders of SODIUM balance

- The normal aged kidney can adjust appropriately in low/high s-Na states but response time is impaired.
- Renal response to dietary Na restriction is blunted due to blunted reabsorption in ascending limb of loop of Henle.
- Proximal Na handling intact.
Elderly patient therefore more prone to sodium wasting and hyponatremia
Renal response to sodium load

- Sluggish
- Reduced natriuresis
- Augmented response to AT11 with greater fall in renal perfusion, impaired natriuresis and augmented kaliuresis.
- Altered response to all vasoactive mediators
Hyponatremia

- Most common electrolyte disorder in elderly
- 1/4 of all hospitalized patients
Causes of hyponatremia in elderly:

1. Decreased ability to excrete free water
2. Water intoxication in setting of diuretic therapy
3. Over secretion of AVP
4. Hypervolemic hyponatremia due to CCF
5. Antidepressants, NSAIDS etc.
Hypernatremia:

- Especially frail + institutionalized
- Failure to recognize thirst
Potassium balance:

- Reduced total body potassium - 20%
- Due to: reduced muscle mass, altered cell membranes, nutritional deficiency, inability of kidney to conserve potassium
Hypokalemia

- 11% of elderly at OPD
- Diuretic therapy
Hyperkalemia

- Not common
- But more prone to high K+ due to NSAIDS, K-supplements and TMX-S, ACE-inh, ARB, Spirinolactone
Acid-base

- Decrease in s-bicarb with age
- Reduced ability to excrete acid load to reduced nephron number
Ca+, PO4+ and Mg+

- S-Ca, P04, i-Ca, Mg and PTH remain normal
- Tendency to slightly higher PTH
Ca+ metabolism is significantly impaired:

- Reduced intestinal Ca absorption
- Reduced renal 1alpha-hydroxylase activity
- Reduced 1,25(OH)2VitD3 activity
- Reduced intestinal adaptation to dietary Ca-restriction
Low Vit-D levels common in frail elderly:

- Lack of sun exposure
- Dietary deficiency
- Impaired conversion to calcitriol
- Changes in GH and ILGF-1
- Renal Ca absorption remains unchanged
Phosphate:

- Reduced renal tubular reabsorption of PO₄
- Decreased intestinal PO₄ absorption
- Impaired renal adaptation to dietary PO₄ restriction
- Little effect in serum levels
- Mg levels do not change
Kidney disease in elderly:

- Little threat to well-being
- 50% of normal is adequate to sustain good renal health
- Acquired kidney disease can accelerate natural decline in GFR
- Incidence of primary kidney disease same as for young – spectrum of disease differ
Nephrotic syndrome: membranous, proliferative and RPGN, FSGS

Substantial proportion of minimal change

Nephritic syndrome: RPGN

Secondary kidney disease increases with age: hpt, DM, CCF etc

Vasculitis and deposition disease: amyloid, light chain deposit, fibrillary GN
AKI in elderly:

- Enhanced susceptibility to AKI secondary to: septic shock, volume depletion, nephrotoxins, obstructive causes.

- Nephrotoxic causes more common than shock associated AKI: aminoglycosides, NSAIDS, ACE-inhibitors
Elderly more prone to pre-renal failure: reduced sodium intake, diuretic use, salt wasting (predisposed to dehydration)

More prone to contrast induced nephropathy due to volume depleted state

More prone to complications and toxicity of drugs and procedures
<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>% OF BIOPSY</th>
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</thead>
<tbody>
<tr>
<td>Pauci-immune GN</td>
<td>31.2</td>
</tr>
<tr>
<td>AIN</td>
<td>18.6</td>
</tr>
<tr>
<td>ATN + nephrotic</td>
<td>7.5</td>
</tr>
<tr>
<td>Atheroemboli</td>
<td>7.1</td>
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<tr>
<td>ATN necrosis alone</td>
<td>6.7</td>
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<tr>
<td>Light chain cast</td>
<td>5.9</td>
</tr>
<tr>
<td>Post-infectious GN</td>
<td>5.5</td>
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<tr>
<td>Anti-GBM GN</td>
<td>4.0</td>
</tr>
<tr>
<td>IgAN H-S + purpura</td>
<td>3.6</td>
</tr>
<tr>
<td>Non-diagnostic</td>
<td>9.9</td>
</tr>
</tbody>
</table>
CKD in elderly

- Prevalence highest in older age groups
- More elderly with ESRD enter dialysis every year esp after age 75
- In addition to direct burden of CKD ESRD at 75 increases risk of death 3 fold
Elderly less likely to be transplanted

Significant impact on health budget

More likely to die of CVS disease than progress to ESRD: CKD 52% risk of death in 1 year compared to 26% without CKD

Aggressive management of risk factors and CVS disease
Hypertension in the elderly

"I'm sure if I moved to a fresh water environment, my hypertension would abate."
Older patients have unique needs and co-morbid conditions that make selection of appropriate medication important.

Minimize side effects

Minimize cost

Poor compliance
The elderly are more prone to side effects of treatment and this has to be kept in mind.
Proper technique for measuring blood pressure

Provide written and verbal feedback
Why treat Hpt

- Decreased stroke 35-40%
- Decreased MI 20-25%
- Decreased CCF 50%
Goal

- < 140/90
- < 130/80 in diabetes or renal disease
- < 160 systolic for ISH
- Over 50 yrs - control of systolic more important
Treatment

- Lifestyle modifications 4-6 months
- If BP 20mmHg above systolic goal or diastolic 10mmHg above diastolic - start with drug therapy initially
- Initial drug - Thiazide diuretic (diuretic, ACE/ARB, long acting CCB)
Thiazides

- 6.25 - 50mg

- Remember hypoK+, HypoNa+, hyperuricemia, hyperglycemia

- Low dose and replace K+ helps to prevent hyperglycemia

- Renal failure, pancreatitis

- Monitor s-K+ and creatinine once or twice per year

- Chlorthalidone superior to HCTZ
<table>
<thead>
<tr>
<th>Medication</th>
<th>Co-morbidity</th>
<th>Avoid with</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide</td>
<td>1st line for all</td>
<td>Gout, hypoNa+</td>
</tr>
<tr>
<td>CCB</td>
<td>CAD, DM</td>
<td>Heart Block</td>
</tr>
<tr>
<td>ACE</td>
<td>CAD, post MI, CHF, DM, CRF</td>
<td>Angioedema</td>
</tr>
<tr>
<td>ARB</td>
<td>CHF, DM, CRF</td>
<td>Angioedema</td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>CAD, post MI, CHF, DM</td>
<td>Asthma, heart block</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>CHF, post MI</td>
<td>Hyperkalemia</td>
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</tbody>
</table>
START LOW and GO SLO but GO

This will help avoid side effects and ensure compliance

Most will eventually require standard doses

One month follow-up intervals till goal reached then 3-6 monthly
ISH

- Enough data to justify systolic BP > 160
- Between 140 and 159 depends on co-morbidity
- Related to large vessel stiffness
- Diastolic related in increased small vessel resistance
Oldest of old:

- HYVET trial
- Patients > 80 with systolic > 160
- Target < 150/80
- Indapamide +/- perindopril
- 21% reduction in mortality - mainly stroke
- 64% reduction in CCF
- Few adverse events
Widened pulse pressure:

- Independent risk for CV events
- 10mmHg increase causes 24% increase in stroke and 32% in CHF
- THE LOWER THE DIASTOLIC, THE HIGHER THE RISK
- Diuretics lower pulse pressure
- Beta-blockers increase pulse pressure
Finally!

- Minimize polypharmacy
- Simple treatment plan
- Inexpensive drugs
- Educate and empower patients
- Team approach - pharmacist, nurse
It's windy today!

No, it's Thursday!

So am I! Let's have a beer!