General Internal Medicine 2-Day Review Course

19-20 September 2019

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Day 1 Session 6: Nephrology

Day 1 TEACHING SESSIONS

- Approach to patient care
- Documentation
- Cardiology overview
- Pulmonology overview
- Gastroenterology overview
- Nephrology overview
- Rheumatology overview
- Endocrinology overview
- Neurology overview
- Overlapping chronic illness

Day 2 TEACHING SESSIONS

- Bedside teaching
- Hospital medicine
- Hospital medicine pearls
- Geriatrics
- Infectious disease overview
- Surviving Sepsis campaign
- HDU/ICU basics
- Mental Health and whole-person care

Day 1: Teaching Sessions

- Approach to patient care
- Documentation
- Organ system review
  - Cardiology overview
  - Pulmonology overview
  - Gastroenterology overview
  - Nephrology overview
  - Rheumatology overview
  - Endocrinology overview
  - Neurology overview
- Overlapping chronic illness

Nephrology

- Renal function
  - AKI
  - CKD
  - Renal replacement therapy
- Medication adjustment in renal impairment
- Hypertension
  - Likely highest contributor to CKD in Malawi
  - Adjustment needed depending on fluid balance / AKI
- Volume status and pulmonary edema

Acute Kidney Injury

- Drug induced
- Secondary to hypovolemia
- Glomerular damage
- Hypertensive emergency

Acute Kidney Injury

- Drug induced
  - Diuretics
  - ACE-I and ARB
  - Antibiotics
  - NSAIDs (brufen, diclofenac)
  - ARVs
- Secondary to hypovolemia
- Glomerular damage
- Hypertensive emergency

Acute Kidney Injury

- Drug induced
- Secondary to hypovolemia
  - Insensitive loss (diarrhea, fever, ambient temp/exertion, vomiting)
  - Heart failure, liver disease
  - Shock (distributive, cardiogenic, hemorrhagic, obstructive)
  - Multi-organ failure / systemic
- Glomerular damage
- Hypertensive emergency

Acute Kidney Injury

- Drug induced
- Secondary to hypovolemia
- Glomerular damage
  - Nephritic syndrome
  - Nephrotic syndrome
- Hypertensive emergency

- The following slides are selected from presentations found online

Renal Failure

Michele Ritter, M.D.

Argy Resident – February, 2007

Assessment of Renal Function

- **Glomerular Filtration Rate (GFR)**
  - = the volume of water filtered from the plasma per unit of time.
  - Gives a rough measure of the number of functioning nephrons
  - Normal GFR:
    - Men: 130 mL/min./1.73m2
    - Women: 120 mL/min./1.73m2
  - Cannot be measured directly, so we use **creatinine** and **creatinine clearance** to estimate.

Assessment of Renal Function (cont.)

- **Creatinine**
  - A naturally occurring amino acid, predominately found in skeletal muscle
  - Freely filtered in the glomerulus, excreted by the kidney and readily measured in the plasma
  - As plasma creatinine increases, the GFR exponentially decreases.
  - Limitations to estimate GFR:
    - Patients with decrease in muscle mass, liver disease, malnutrition, advanced age, may have low/normal creatinine despite underlying kidney disease
    - 15-20% of creatinine in the bloodstream is not filtered in glomerulus, but secreted by renal tubules (giving overestimation of GFR)
    - Medications may artificially elevate creatinine:
      - Trimethroprim (Bactrim)
      - Cimetidine

Assessment of Renal Function (cont.)

- **Creatinine Clearance**
  - Best way to estimate GFR
  - **GFR = (creatinine clearance) x (body surface area in m^2/1.73)**
  - Ways to measure:
    - 24-hour urine creatinine:
      - **Creatinine clearance = (Ucr x Uvol)/ plasma Cr**
    - Cockcroft-Gault Equation:
      - $$\text{CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{lean body weight [kg]}}{\text{Cr [mg/dL]} \times 72} \times 0.85 \text{ if female}$$
      - Limitations: Based on white men with non-diabetes kidney disease
    - Modification of Diet in Renal Disease (MDRD) Equation:
      - **GFR (mL/min./1.73m2) = 186 X (SCr)-1.154 X (Age)-0.203 X (0.742 if female) X (1.210 if African-American)**

Major causes of Kidney Failure

- Prerenal Disease
- Vascular Disease
- Glomerular Disease
- Interstitial/Tubular Disease
- Obstructive Uropathy

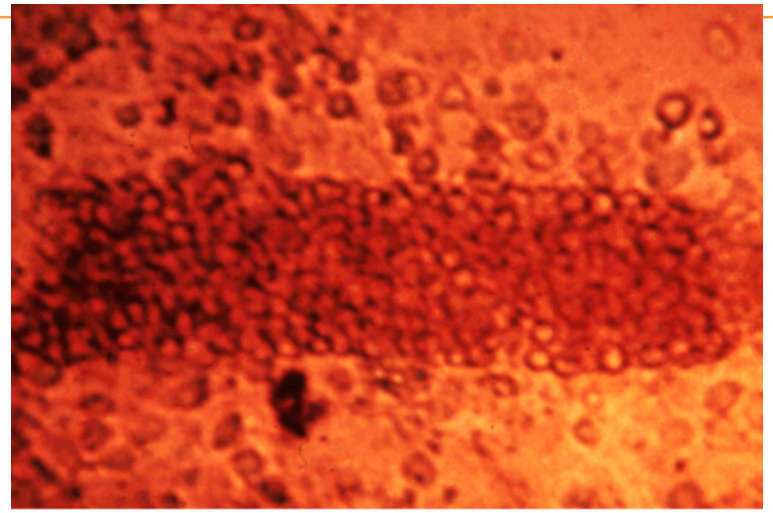
Vascular Disease

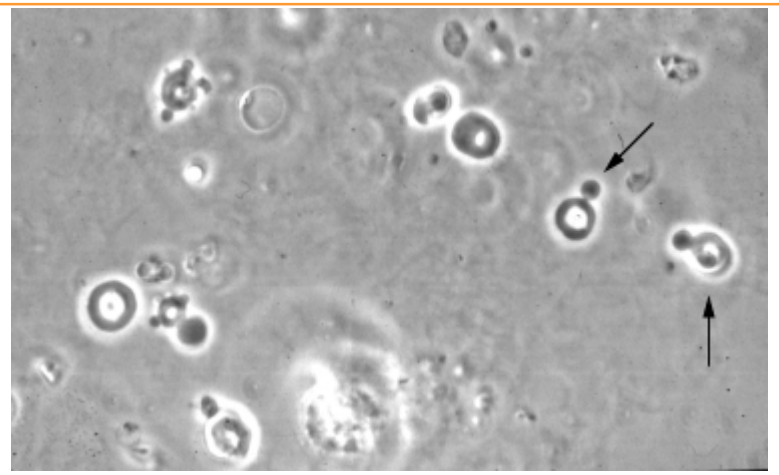
- **Acute**
  - **Vasculitis – Wegener's granulomatosis**
  - **Thromboembolic disease**
  - **TTP/HUS**
  - **Malignant hypertension**
  - **Scleroderma renal crisis**
- **Chronic**
  - **Benign hypertensive nephrosclerosis**
    - Intimal thickening and luminal narrowing of the large and small renal arteries and the glomerular arterioles usually due to hypertension.
    - Most common in African Americans
    - Treatment:
      - **Hypertension control**
  - **Bilateral renal artery stenosis**
    - should be suspected in patients with acute, severe, or refractory hypertension who also have otherwise unexplained renal insufficiency
    - Treatment:
      - Medical therapy, surgery, stents.

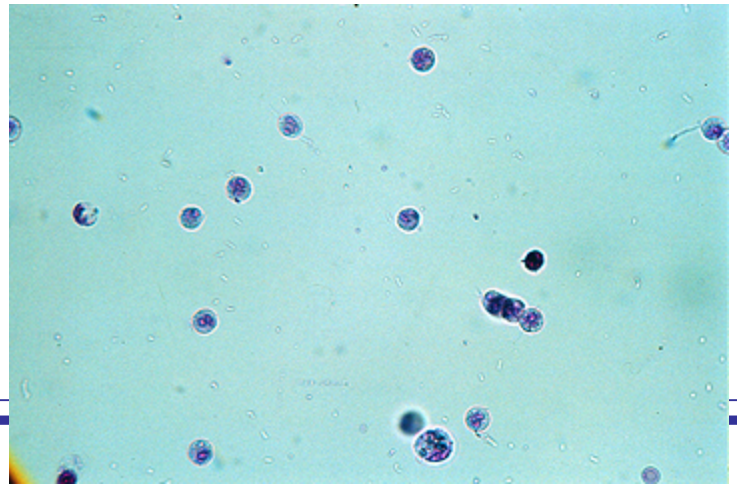
Glomerular Disease

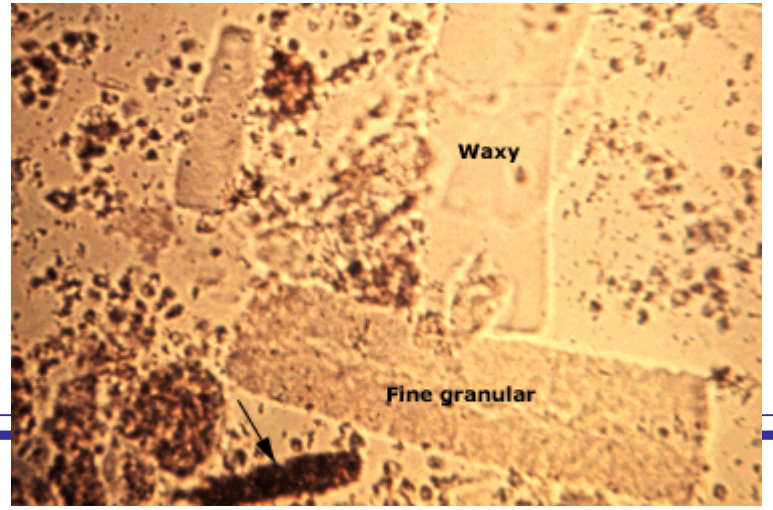
- Nephritis
  - Inflammation seen on histologic exam
  - Active sediment: Red cells, white cells, granular casts, red cell casts
  - Variable degree of proteinuria (< 3g/day)
- Nephrotic
  - No inflammation
  - Bland sediment: No cells, fatty casts
  - Nephrotic range proteinuria (>3.5 g/day)
  - Nephrotic syndrome = proteinuria + hyperlipidemia + edema

Glomerulonephritis

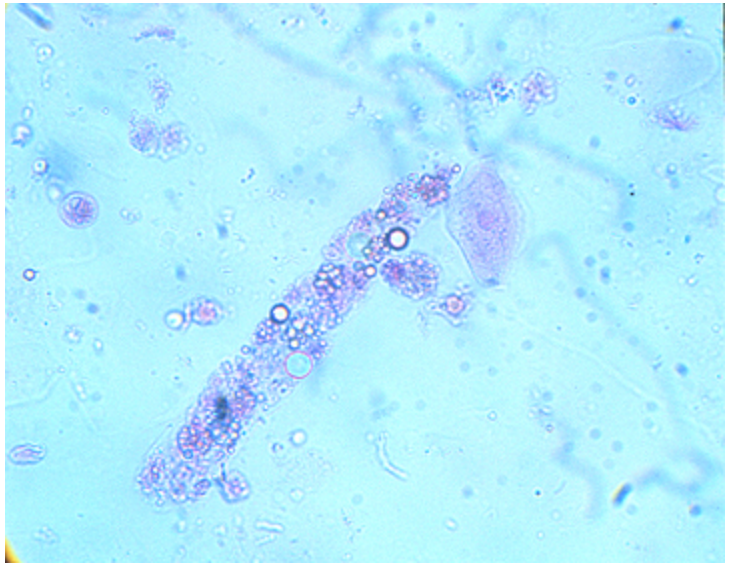








Nephrotic



Glomerular Disease -- Glomerulonephritis

- Postinfectious glomerulonephritis
  - Group A Strep Infection
- Membranoproliferative glomerulonephritis:
  - infective endocarditis
  - Systemic lupus erythematosus
  - Hepatitis C virus
- Rapidly progressive glomerulonephritis
  - IgA nephropathy
    - Infections: CMV, Staph. Aureus, H. influenzae
  - SLE
  - Goodpasture syndrome (anti-GBM)
  - Henoch-Schönlein purpura
  - Wegener granulomatosis
  - Polyarteritis nodosa
- Vasculitis (cryoglobulinemia)

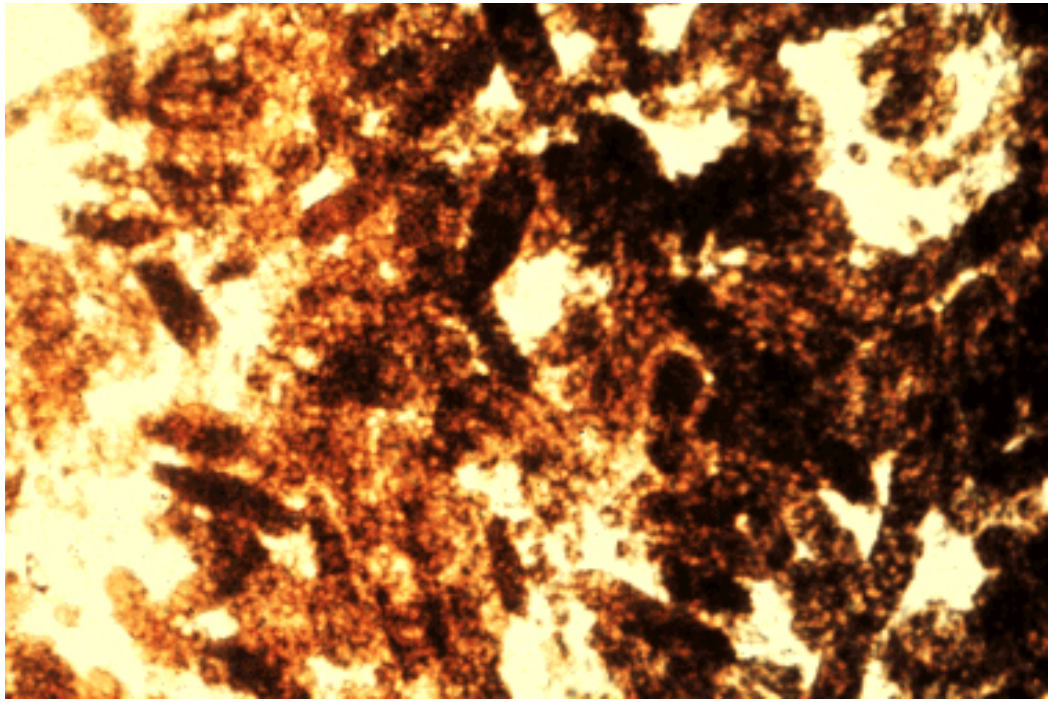
Glomerular Disease – Nephrotic Syndrome

- Minimal Change Disease
  - **NSAIDS**
  - **Paraneoplastic (Hodgkin's Lymphoma)**
- Focal glomerulosclerosis
  - **HIV**
  - Massive Obesity
  - NSAIDS
- Membranous nephropathy
  - **NSAIDS**, penicillamine, gold
  - Etanercept, infliximab
  - **SLE**
  - Hep. C, Hep. B
  - **Malignancy (usually of GI tract or lung)**
  - GVHD
  - s/p renal transplant
- Mesangial proliferative glomerulonephritis
- Diabetic nephropathy
- Post-infectious glomerulonephropathy (later stages)
- Amyloidosis
- IgA nephropathy
  - Infections: **HIV**, CMV, *Staph. aureus, Haemophilus parainfluenza*
  - Celiac disease
  - Chronic Liver disease

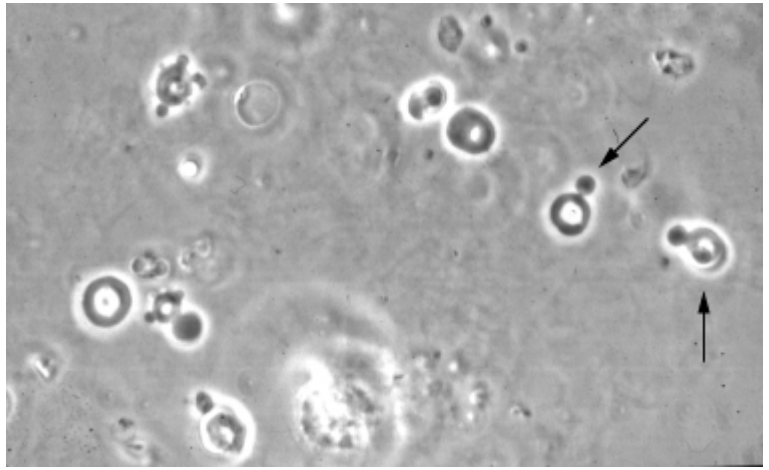
Interstitial/Tubular Disease

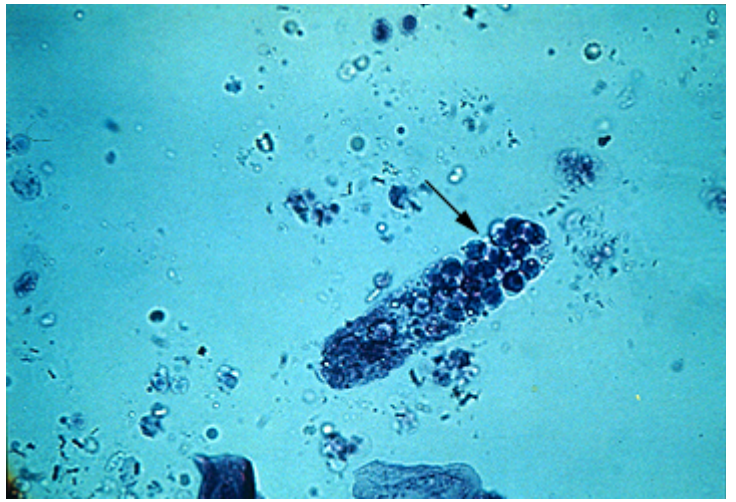
- Acute:
  - **Acute Tubular Necrosis**:
    - One of the most causes of acute renal failure in hospitalized patients
    - Causes:
      - Hypotension, Sepsis
      - Toxins: Aminoglycosides, Amphotericin, Cisplatin, Foscarnet, Pentamadine, **IV contrast**
      - **Rhabdomyolysis** (heme-pigments are toxins)
    - Urine sediment: **muddy brown granular casts**
  - **Acute Interstitial Nephritis**:
    - Causes:
      - Drugs: Antibiotics, Proton-pump inhibitors, **NSAIDS**, allopurinol
      - Infections: Legionella, Leptospirosis
      - Auto-immune disorders
    - Urine sediment: **urine eosinophils** (but not always present), white blood cells, red blood cells, white cell casts
  - **Cast Nephropathy** – Multiple Myeloma
    - Tubular casts – PAS-negative, and PAS-positive (Tamm-Horsefall mucoprotein)

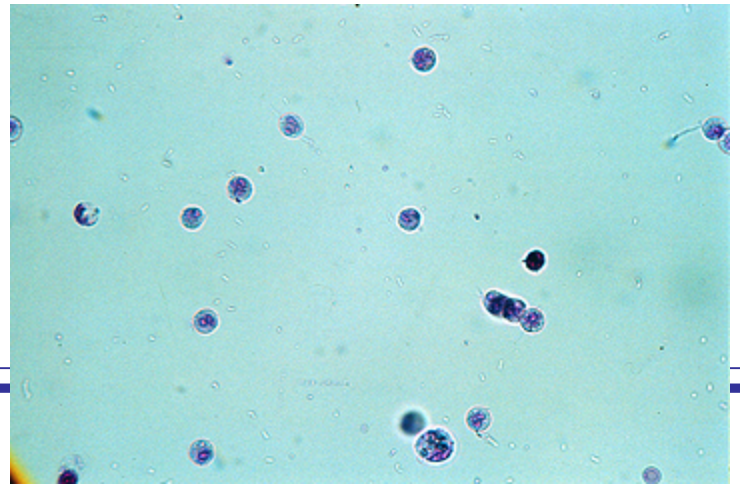
Acute Tubular Necrosis- *muddy brown casts*



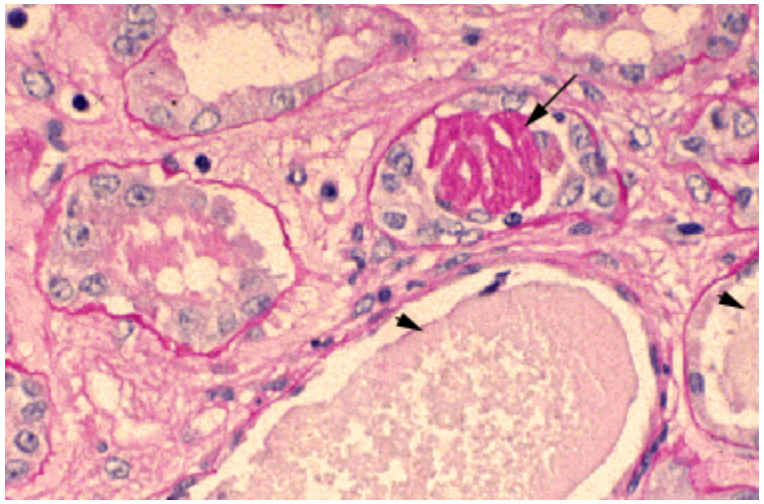
Acute Interstitial Nephritis

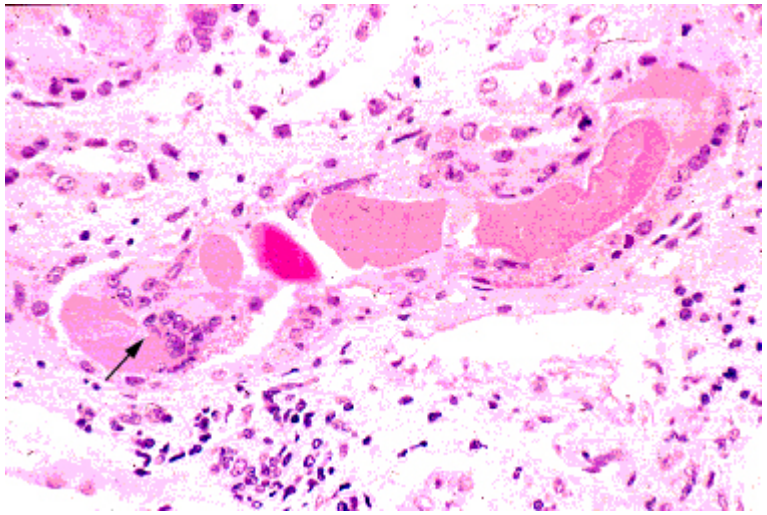






Cast nephropathy – Multiple myeloma
tubular casts





Interstitial Tubular Disease

- Chronic
  - **Polycystic Kidney Disease**
  - **Hypercalcemia**
  - **Autoimmune disorders**
    - Sarcoidosis
    - Sjögren’s syndrome

Obstructive Uropathy

- Obstruction of the urinary flow anywhere from the renal pelvis to the urethra
- Can be acute or chronic
- Most commonly caused by tumor or prostatic enlargement (hyperplasia or malignancy)
- Need to have bilateral obstruction in order to have renal insufficiency

Chronic Kidney Disease

- = a GFR of < 60 for 3 months or more.
- Most common causes:
  - Diabetes Mellitus
  - Hypertension
- Management:
  - Blood pressure control!
  - Diabetic control!
  - Smoking cessation
  - Dietary protein restriction
  - Phosphorus lowering drugs/ Calcium replacement
    - Most patients have some degree of hyperparathyroidism
  - Erythropoietin replacement
    - Start when Hgb < 10 g/dL
  - Bicarbonate therapy for acidosis
  - Dialysis?

Stages of Chronic Kidney Disease

Stage	*Description*	*GFR (mL/min/1.73 m2)*
1	Kidney damage with normal or increased GFR	≥ 90
2	Kidney damage with mildly decreased GFR	60-89
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Kidney Failure	< 15

Acute Renal Failure

- An abrupt decrease in renal function sufficient to cause retention of metabolic waste such as urea and creatinine.
- Frequently have:
  - Metabolic acidosis
  - Hyperkalemia
  - Disturbance in body fluid homeostasis
  - Secondary effects on other organ systems

Acute Renal Failure

- Most community acquired acute renal failure (70%) is **prerenal**
- Most hospital acquired acute renal failure (60%) is due to ischemia or nephrotoxic tubular epithelial injury (**acute tubular necrosis**).
  - Mortality rate 50-70%

Risk factor for acute renal failure

- Advanced age
- Preexisting renal parenchymal disease
- Diabetes mellitus
- Underlying cardiac or liver disease

Urine Output in Acute Renal failure

- Oliguria
  - = daily urine output < 400 mL
  - When present in acute renal failure, associated with a mortality rate of 75% (*versus 25% mortality rate in non-oliguric patients)*
    - Most deaths are associated with the underlying disease process and infectious complications
- Anuria
  - No urine production
  - Uh-oh, probably time for dialysis

Most common causes of ACUTE Renal Failure

- Prerenal
- Acute tubular necrosis (ATN)
- Acute on chronic renal failure (usually due to ATN or prerenal)
- Obstructive uropathy
- Glomerulonephritis/Vasculitis
- Acute Interstitial nephritis
- Atheroemboli

Assessing the patient with acute renal failure (cont.)

- Family History:
  - Cancers?
  - Polycystic kidney disease?

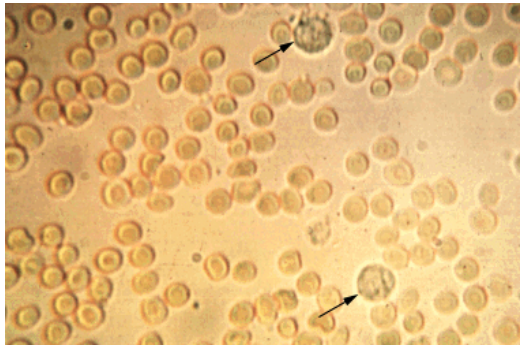
- Meds:
  - Any non-compliance with diabetic or hypertensive meds?
  - Any recent antibiotic use?
  - Any NSAID use?

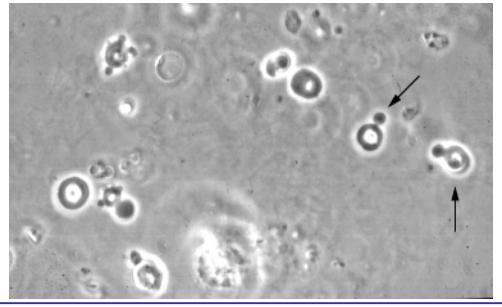
Assessing the patient with acute renal failure -- Radiology

- **Renal Ultrasound**
  - Look for signs of hydronephrosis as sign of obstructive uropathy.

Assessing the patient with acute renal failure – **Urinalysis**

- Hematuria
  - Non-glomerular:
    - Urinary sediment: intact red blood cells
    - Causes:
      - Infection
      - Cancer
      - Obstructive Uropathy
  - Rhabdomyolysis
    - myoglobinuria; **Hematuria with no RBCs**
  - Glomerular:
    - Urine sediment: dysmorphic red blood cells, red cell casts
    - Causes:
      - **Glomerulonephritis**
      - **Vasculitis**
      - **Atheroembolic disease**
      - **TTP/HUS** (thombotic microangiopathy)

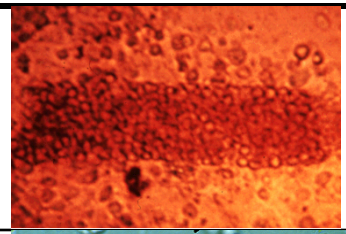
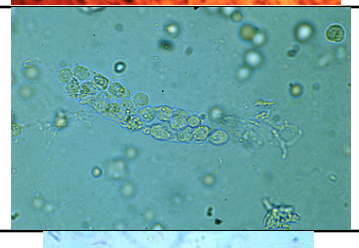
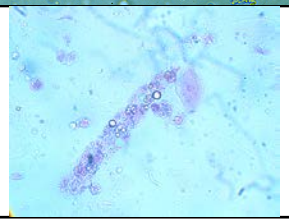
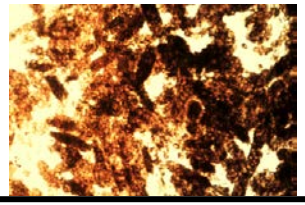




Assessing Patient with Acute Renal Failure – **Urinalysis** (cont.)

- Protein
  - Need microscopic urinalysis to see microabluminemia
  - Can check 24-hour urine protein collection
    - Nephrotic syndrome - ≥ 3.5 g protein in 24 hours
  - **Albuminuria**
    - **Glomerulonephritis**
    - **Atheroembolic disease**
    - **(TTP/HUS) Thrombotic microangiopathy**
    - **Nephrotic syndrome**
  - **Tubular proteinuria**
    - **Tubular epithelial injury (acute tubular necrosis)**
    - **Interstitial nephritis**

Assessing patient with acute renal failure – **Urinary Casts**

Red cell casts	**Glomerulonephritis** **Vasculitis**	
White Cell casts	**Acute Interstitial nephritis**	
Fatty casts	**Nephrotic syndrome, Minimal change disease**	
Muddy Brown casts	**Acute tubular necrosis**	

Assessing patient with acute renal failure – Renal Biopsy

- If unable to discover cause of renal disease, renal biopsy may be warranted.
- Renal biopsy frequently performed in patient's with history of renal transplant with worsening renal function.

Treatment of Acute Renal Failure

- Treat underlying cause
  - Blood pressure
  - Infections
  - Stop inciting medications
  - Nephrostomy tubes/ureteral stents if obstruction
  - Treat scleroderma renal crisis with ACE inhibitor
- Hydration
- Diuresis (Lasix)
- Dialysis
- Renal Transplant

Indications for Hemodialysis

- Refractory fluid overload
- Hyperkalemia (plasma potassium concentration >6.5 meq/L) or rapidly rising potassium levels
- Metabolic acidosis (pH less than 7.1)
- Azotemia (BUN greater than 80 to 100 mg/dL [29 to 36 mmol/L])
- Signs of uremia, such as pericarditis, neuropathy, or an otherwise unexplained decline in mental status
- Severe dysnatremias (sodium concentration greater than 155 meq/L or less than 120 meq/L)
- Hyperthermia
- Overdose with a dialyzable drug/toxin

Question # 1

- A 82-year old female with a history of Alzheimer's dementia presents from her nursing home with diarrhea for three days. Per nursing home documents, there have been multiple recent outbreaks of C. difficile colitis among their residents.

Question #1

- PMH:
  - Alzheimer’s Dementia
  - Osteoarthritis
- Allergies: PCN
- Meds:
  - Aricept
  - Ibuprofen prn

Question # 1 (cont.)

- Physical Exam:
  - Temp: 36.1, 82/46, 96, 16, 98% on RA
  - Gen.: Slightly lethargic, oriented to self only; in NAD
  - HEENT: very dry mucous membranes
  - CV: RRR; no murmurs
  - Abd.: soft, nontender, NABS
  - Ext.: No LE edema

Question #1 (cont.)

- Labs:
  - WBC: 19.2
  - Hgb.: 11
  - Hct: 32.8
  - Platelets: 202
  - Sodium: 132
  - Potassium: 5.6
  - Chloride: 103
  - Bicarbonate: 18
  - BUN: 32
  - Cr.: 1.8
  - Glucose: 79
  - Urine dipstick:
    - Protein: none
    - Ketones: trace
    - Blood: none
    - Leuk est: none

Question # 1 (cont.)

- What further information would be helpful in evaluating this patient?
- What are some possible diagnoses in this patient?
- What further studies would you like to do?
- What might you see in urinary sediment?

Question # 1 (cont.)

- Urine sodium = 40 mg/dL
- Urine creatinine = 140 mg/dL
- Renal ultrasound: no sign of hydronephrosis

Question # 1 (cont.)

- What kind of renal failure do you think this patient has?
- How would you treat this patient?

Question #2

- A 75-year old woman is admitted to the hospital for confusion. The patient is oriented to person but not time or place. She has a history of cervical cancer, treated with total hysterectomy and radiation 18 months ago. Previous evaluation in her private physician's office 3 months ago showed her serum creatinine concentration was 1.0 mg/dL.

Question #2 (cont.)

- Physical examination shows a temperature of 36.2° C, a regular pulse rate of 98/min., a regular respiration rate of 20/min., and a blood pressure of 110/60 mmHg. There is no orthostasis. There is no neck vein distention at 45 degrees, and the chest is clear. S1 and S2 are normal, without gallop or murmur. Liver span is 18 cm, and the edge is three finger breadths below the right costal margin. The spleen tip is palpable before the left costal margin. There is shifting dullness and bowel sounds are present. There is 2+ pedal edema. Cranial nerves and reflexes are normal, and the neurologic examination did not elicit focal findings.

Question #2 (cont.)

- Labs:
  - Hct: 30.7
  - WBC: 7.3
  - Sodium: 131
  - Potassium: 5.7
  - Chloride: 98
  - Bicarbonate: 15
  - Calcium: 7.2
  - Phosphorus: 6.8
  - BUN: 64
  - Creatinine: 7.3
- Urinalysis:
  - Specific gravity: 1.011
  - Glucose: negative
  - Protein: trace
  - Blood: negative
  - Ketones: negative
  - Microscopic:
    - 0 to 1 RBC per high-power field
    - 0 to 1 WBC /hpf
    - No cellular casts
  - Sodium: 28 mEq/L
  - FENa: 4.1%
  - Osmolality: 168 mosm/kg
  - 4-hour urine volume: 40 mL

Question # 2 (cont.)

- The most appropriate initial step in the clinical management of this patient is:
  - (A) Renal ultrasound
  - (B) Renal Biopsy
  - (C) A trial of normal saline at 300 mL/hr for 2 hours
  - (D) Continuous arteriovenous hemofiltration
  - (E) Renal scintigraphy

Question # 3

- A 45-year old male with a history of metastatic colon cancer is admitted to the hospital for pain control. Patient has known metastases to the spine and pelvis, and has had worsening pain over the last several weeks. Palliative care is consulted and helps with pain control. However, his hospitalization is complicated by nosocomial pneumonia. He underwent a staging CT on Hospital #6, which showed a mild increase in size of spinal, pelvic mets. On hospital day #8, his daily chemistry shows an increase in his creatinine from 1.0 the day before to 1.9.

Question # 3 (cont.)

- PMH:
  - Colon cancer (diagnosed 4 years ago, s/p partial colectomy, chemo., radiation; known mets to liver, lungs, spine/pelvis)
  - GERD
- Allergies: PCN
- Current Meds:
  - Ciprofloxacin
  - Vancomycin
  - Amikacin
  - Dilaudid PCA
  - Pericolace
  - Nexium

Question #3

- What are some possible causes of renal failure in this patient?
- What would you do the urine sediment shows muddy brown casts?
- What would you suspect if urine eosinophils are seen?

- The above slides were selected from presentations found online

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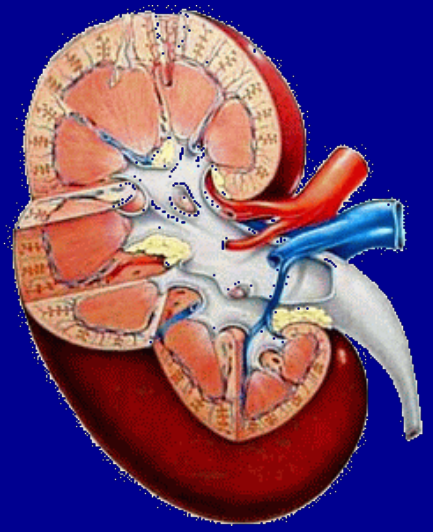
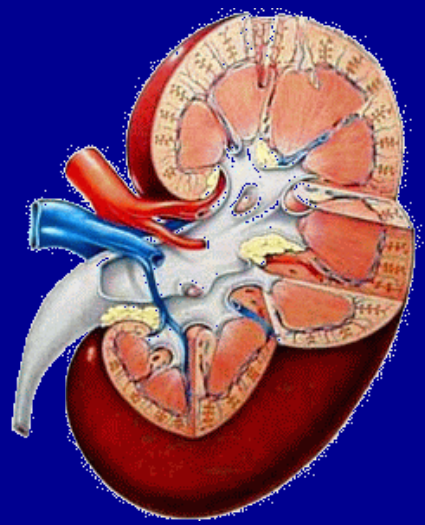
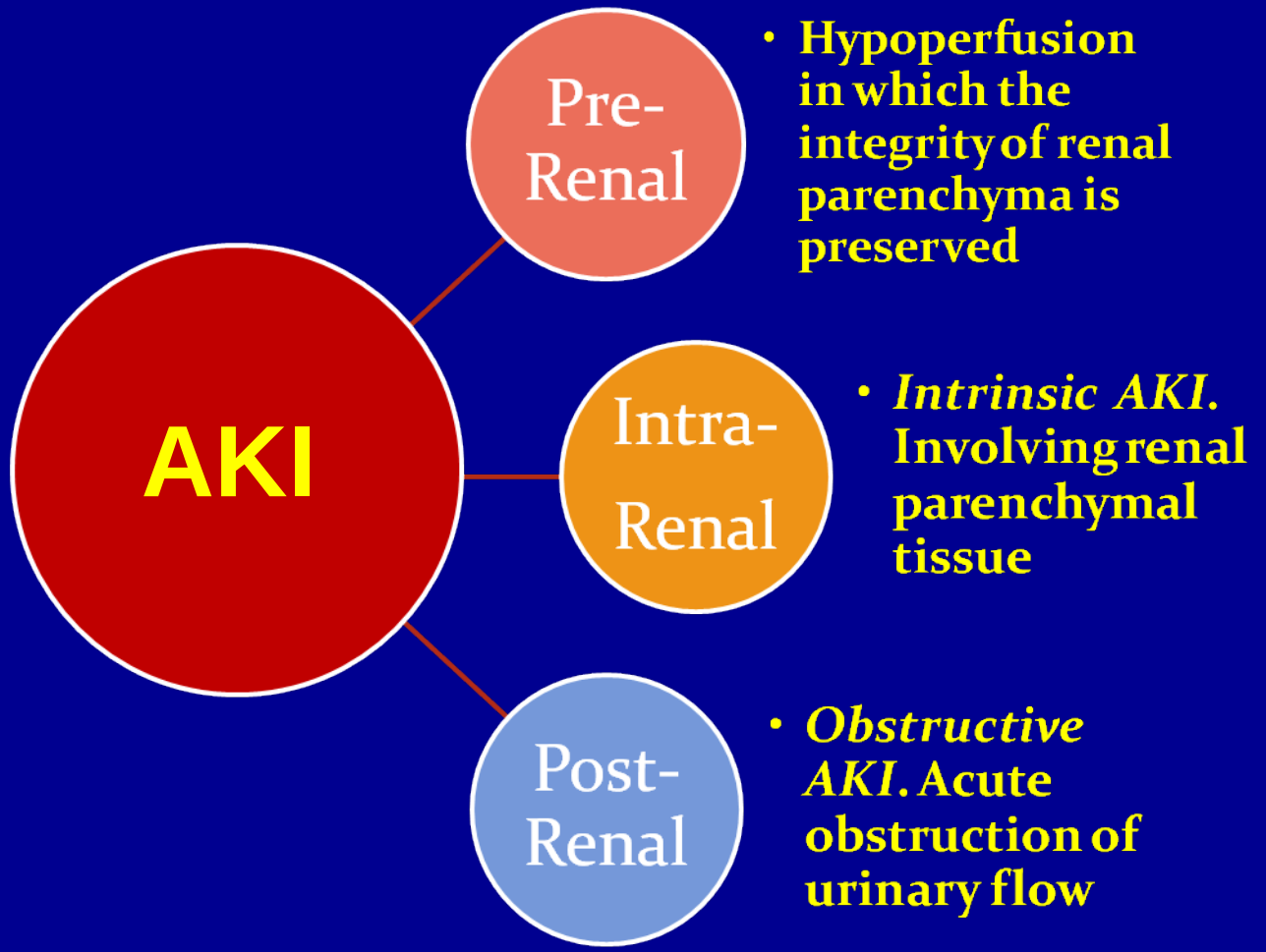
Diuretics and in Acute Kidney Injury



Asad J. Chaudhary M.D.
Clinical Nephrology Fellow
University of Tennessee
Health Science Center.



Etiology of AKI



- **Hypoperfusion in which the integrity of renal parenchyma is preserved**
- ***Intrinsic AKI.*** **Involving renal parenchymal tissue**
- ***Obstructive AKI.*** **Acute obstruction of urinary flow**

Classification of AKI:

- Non Oliguria:
  - Urine output > 400 ml/24hr
- Oliguria:
  - Urine output < 400 ml/24 hr
- Anuria:
  - Urine output < 50 ml/24 hr

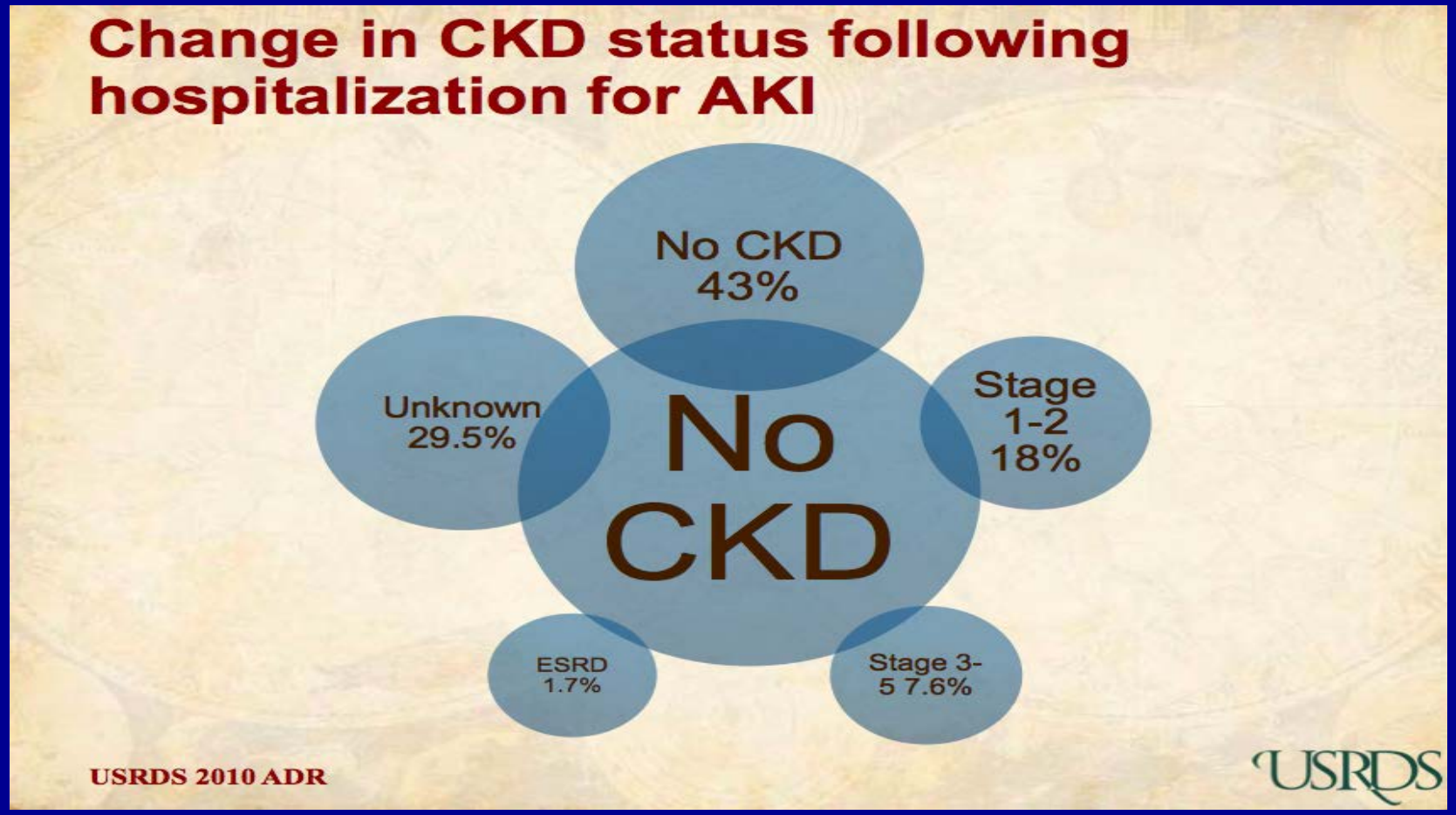
Other terms

- Azotemia:
  - Accumulation of nitrogenous waste
- Uremia:
  - Symptomatic AKI (eg MS changes, loss of appetite, tremors)

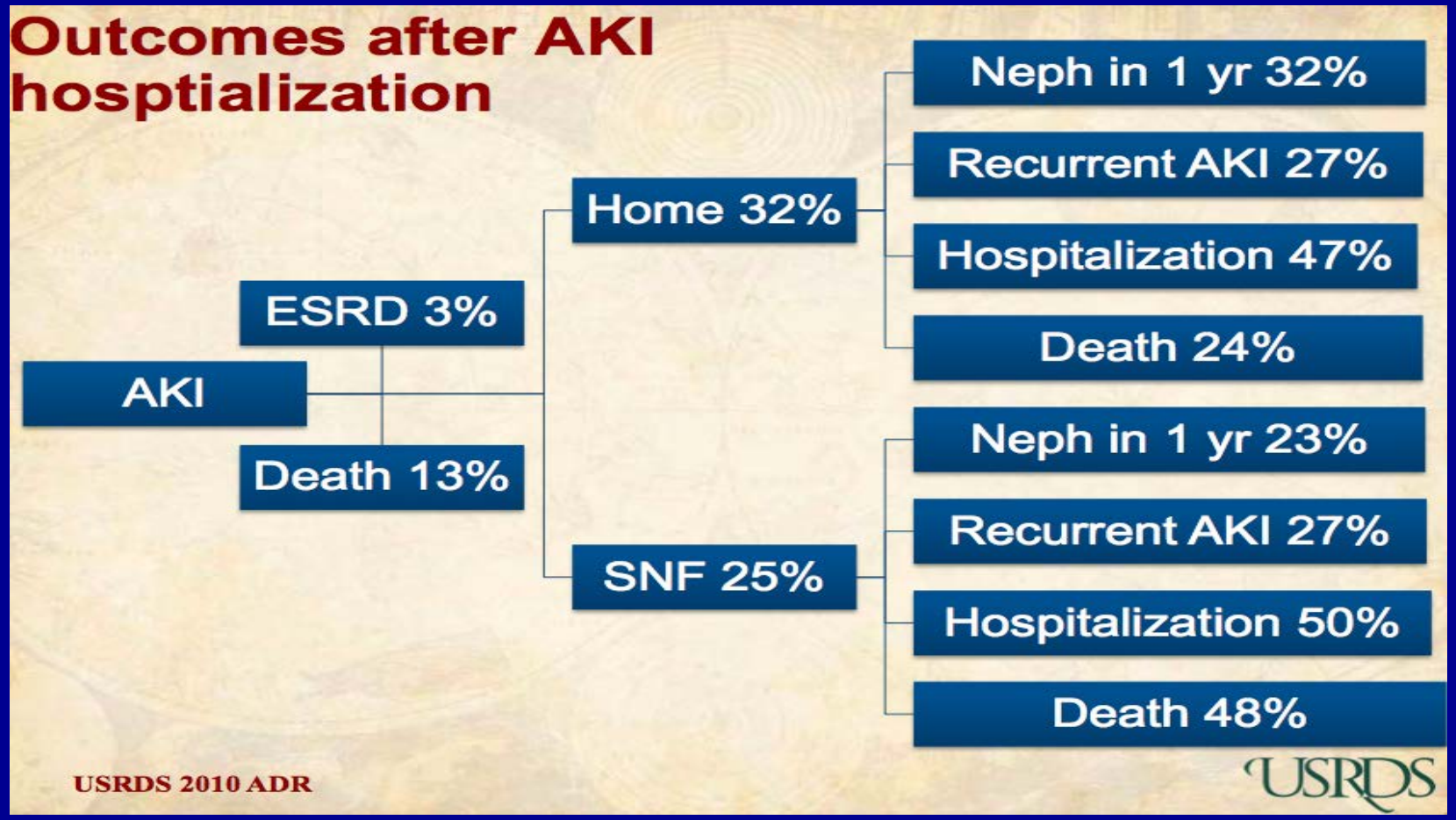
- Oliguria is a well-recognized and poor prognostic indicator in patients with AKI.
- The development of oliguria complicates clinical management, particularly for fluid balance.
- Use of diuretics therefore reflects attempt to convert oliguric state to non-oliguric state.

Bagshaw SM, Bellomo R, Kellum JA. Oliguria, volume over- load, and loop diuretics. Crit Care Med. 2008;36 Suppl:S172-8.
Uchino S. Outcome prediction for patients with acute kidneyinjury. Nephron Clin Pract. 2008;109:c217-23.

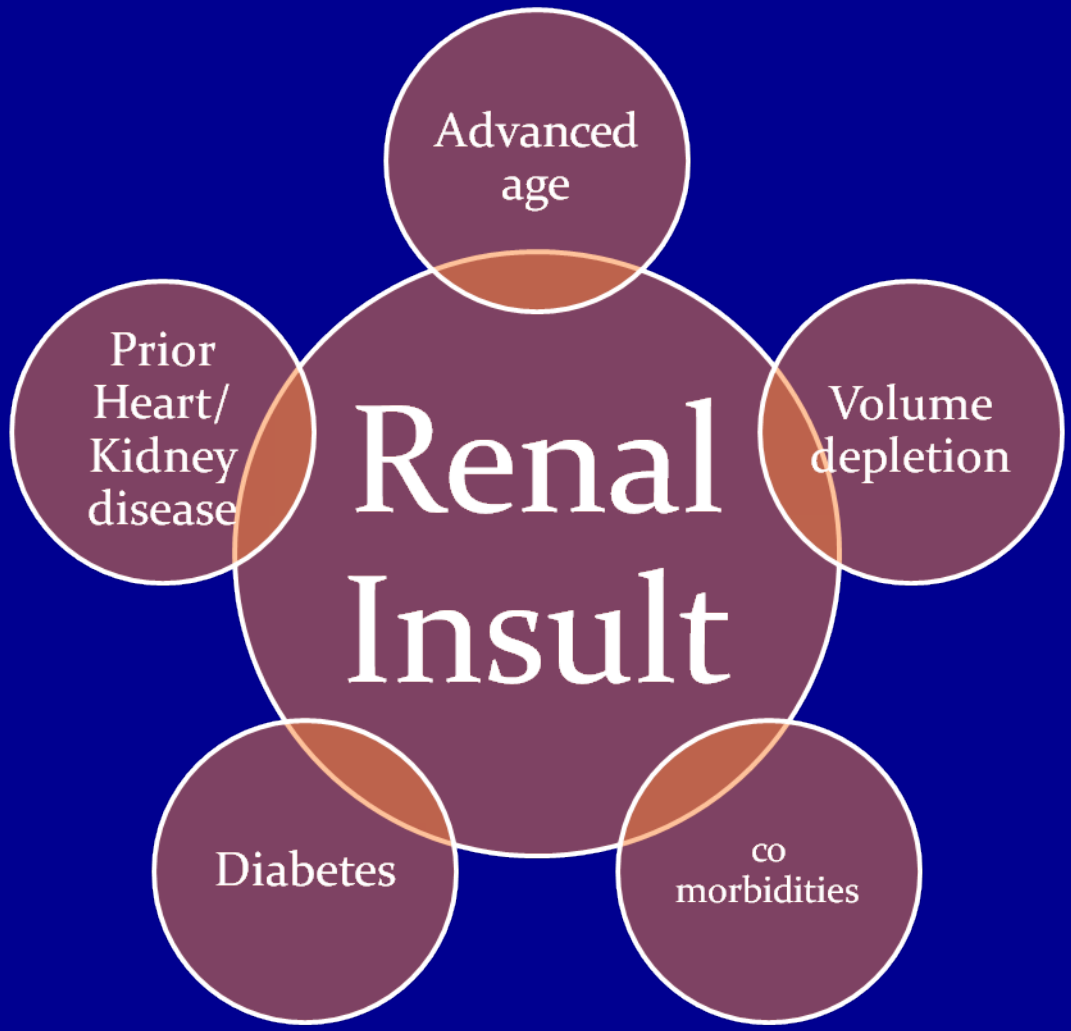
Epidemiology



Epidemiology



High Risk for AKI



Dilemmas of fluid management in acquired AKI

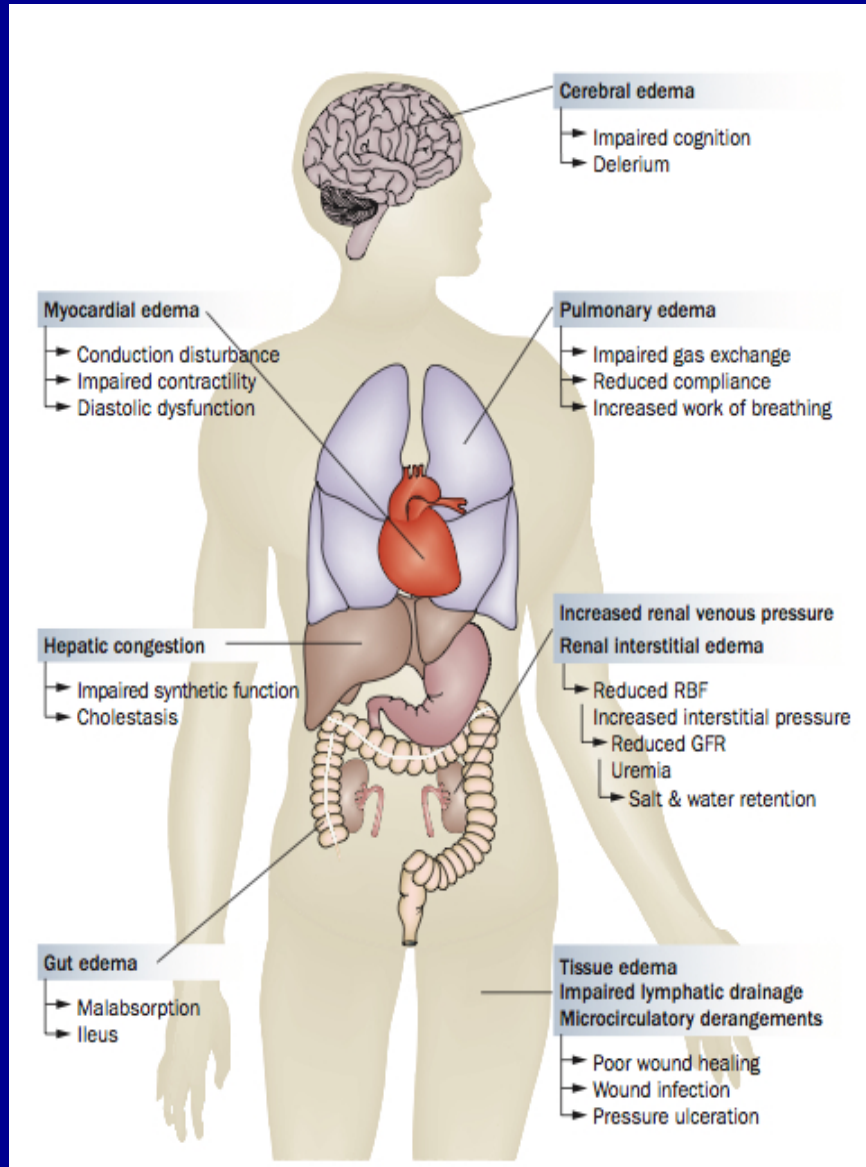


Figure 2 | Pathological sequelae of fluid overload in organ systems. Abbreviations: GFR, glomerular filtration rate; RBF, renal blood flow.

Thank you

Acknowledgement

- Dr. Showkat

- The above slides were selected from presentations found online

Acute renal injury - approach

- When in doubt CKD versus AKI, look at urine sediment, hgb, lytes
- Stop any further injury and promote healing
  - Remove offending agents
  - Correct volume status
  - Optimize BP **AND** glomerular stress
  - Avoid additional nephrotoxins / confounding drugs
  - Remove obstructions
- Time for recovery
  - Volume status – ventilators, non-standard diuretics
  - Temporary renal replacement indications
  - Renally adjust other medications

AKI – practical approach

- Baseline creatinine?
- Current urine output?
- Recent and current medications and supplements?
- Volume status?
- Co-morbidities?
- Electrolytes (U&E, phos, calcium, magnesium)
- FBC (anemia? Leukocytosis?)
- Almost always given a trial of IV fluid boluses

Nephrology

- Renal function
  - AKI
  - CKD
  - Renal replacement therapy
- Medication adjustment in renal impairment
- Hypertension
  - Likely highest contributor to CKD in Malawi
  - Adjustment needed depending on fluid balance / AKI
- Volume status and pulmonary edema

Nephrology - CKD

- Chronic kidney disease is very different from acute kidney injury
- Slowly progressive decline in eGFR
  - DM/HTN most common
  - Affects Africans more than other racial groups
- May include several superimposed episodes of AKI
- CKD and ESRD are disproportionately expensive
- Early intervention does delay need for (renal replacement therapy) RRT
- Survival past 5 years of RRT is low (even in the USA)

- The following slides are selected from presentations found online

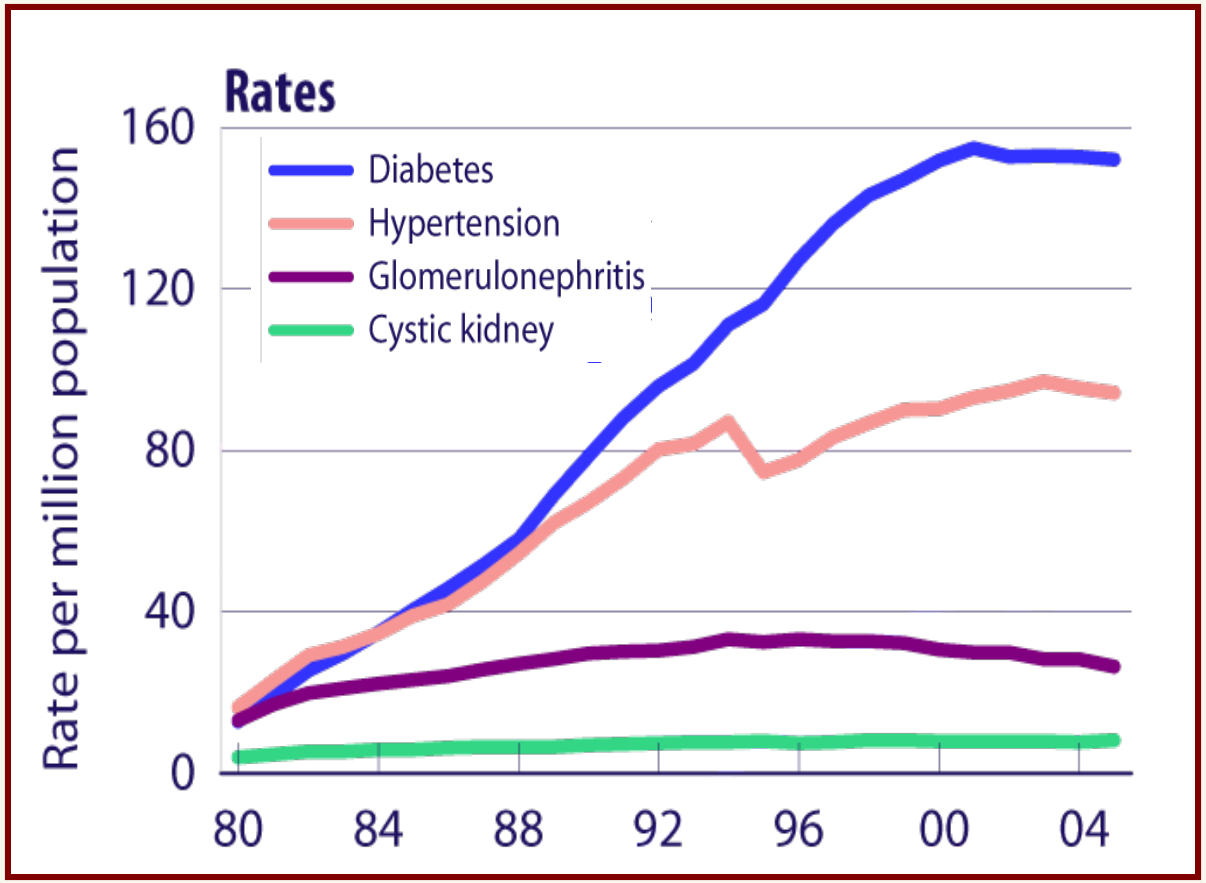
Chronic Kidney Disease

Improving Patient Outcomes in the Primary Care Setting

NKDEP
National Kidney Disease Education Program

ASN
The American Society of Nephrology

Diabetes and hypertension are leading causes of kidney failure



Incident ESRD rates, by primary diagnosis, adjusted for age, gender, & race.

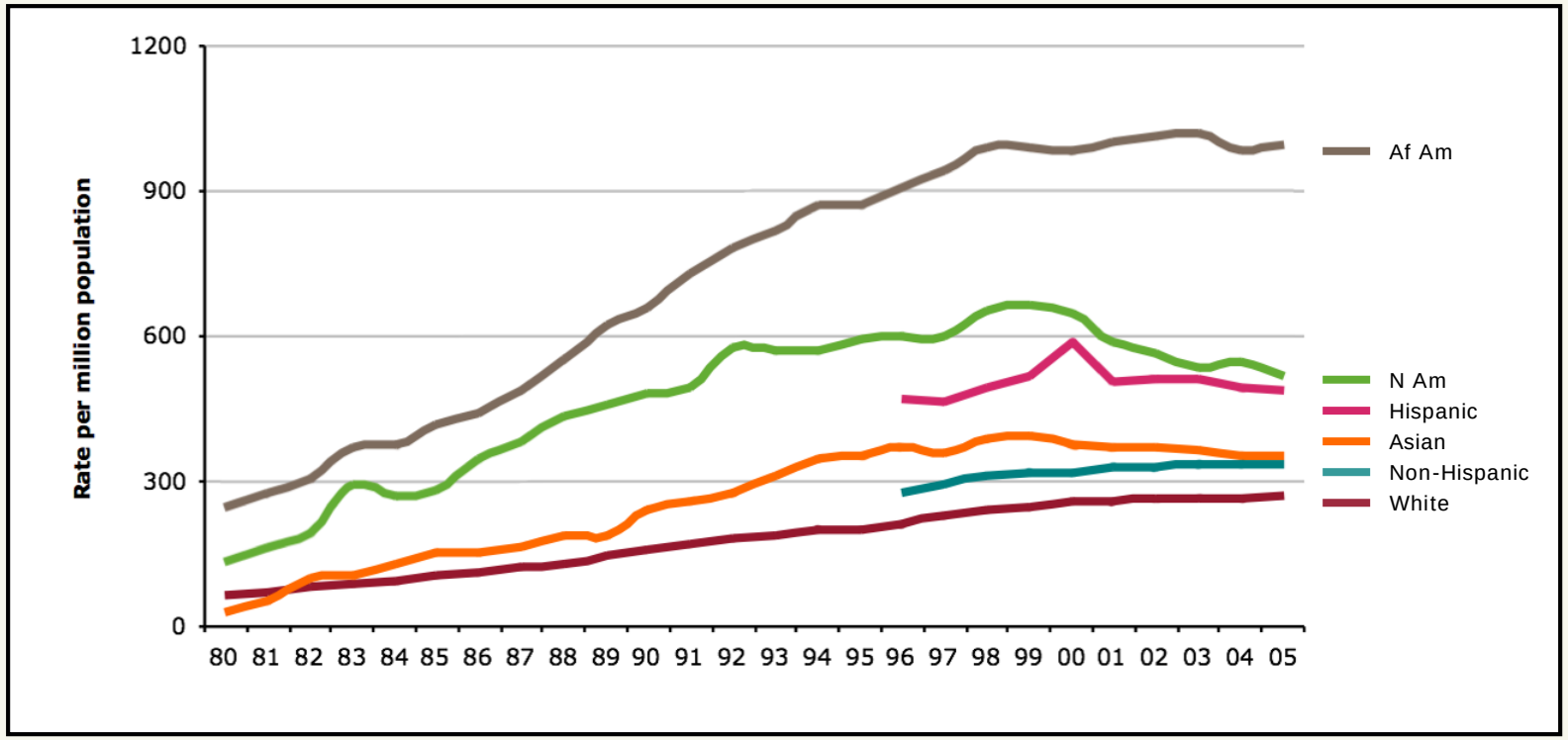
USRDS ADR, 2007

Only certain conditions predispose to CKD

- Diabetes mellitus
- Hypertension
- Cardiovascular disease
- Family members of patients with ESRD

National Kidney Foundation, 2002

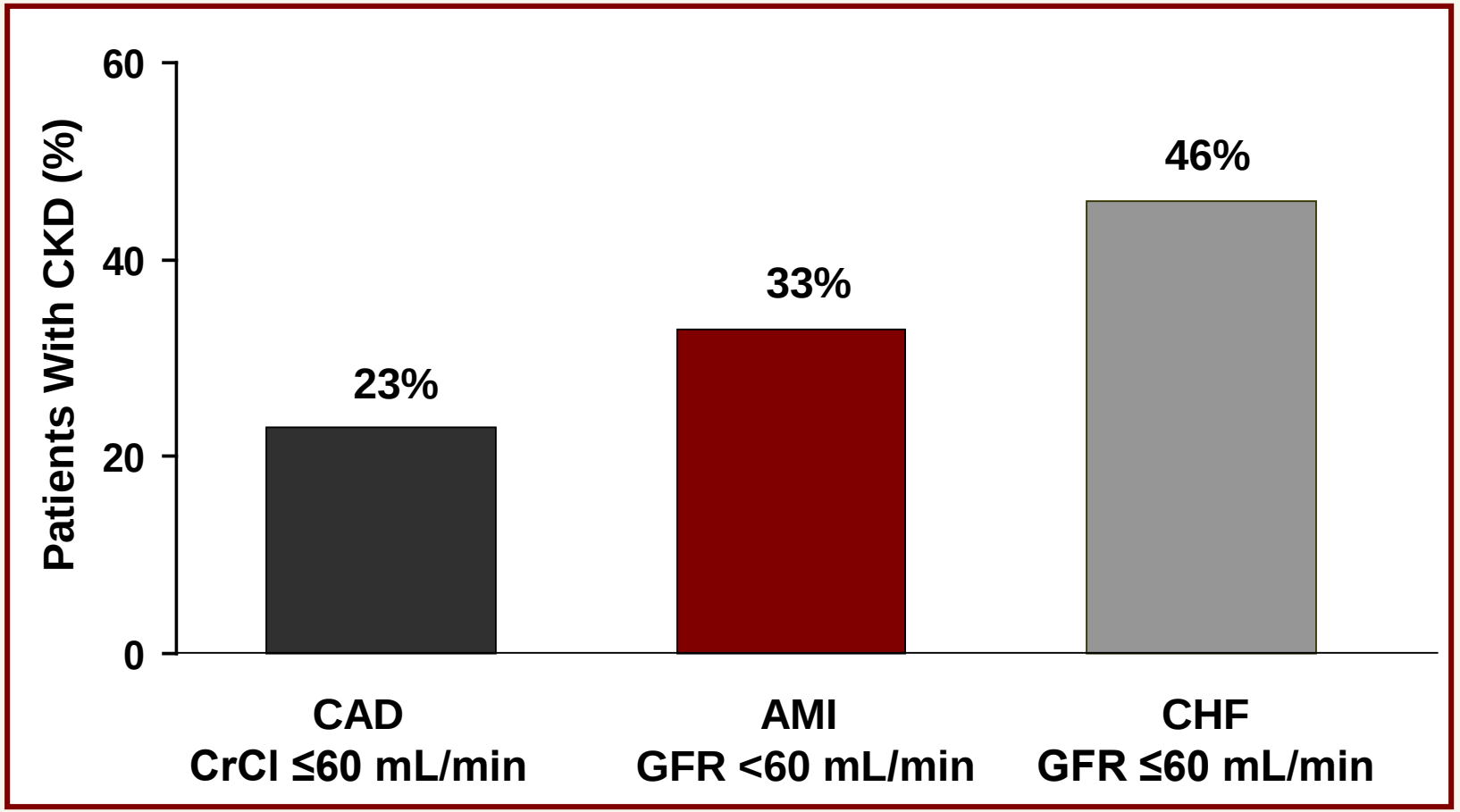
Incidence varies widely by race and ethnicity



Incident ESRD patients; rates adjusted for age & gender.

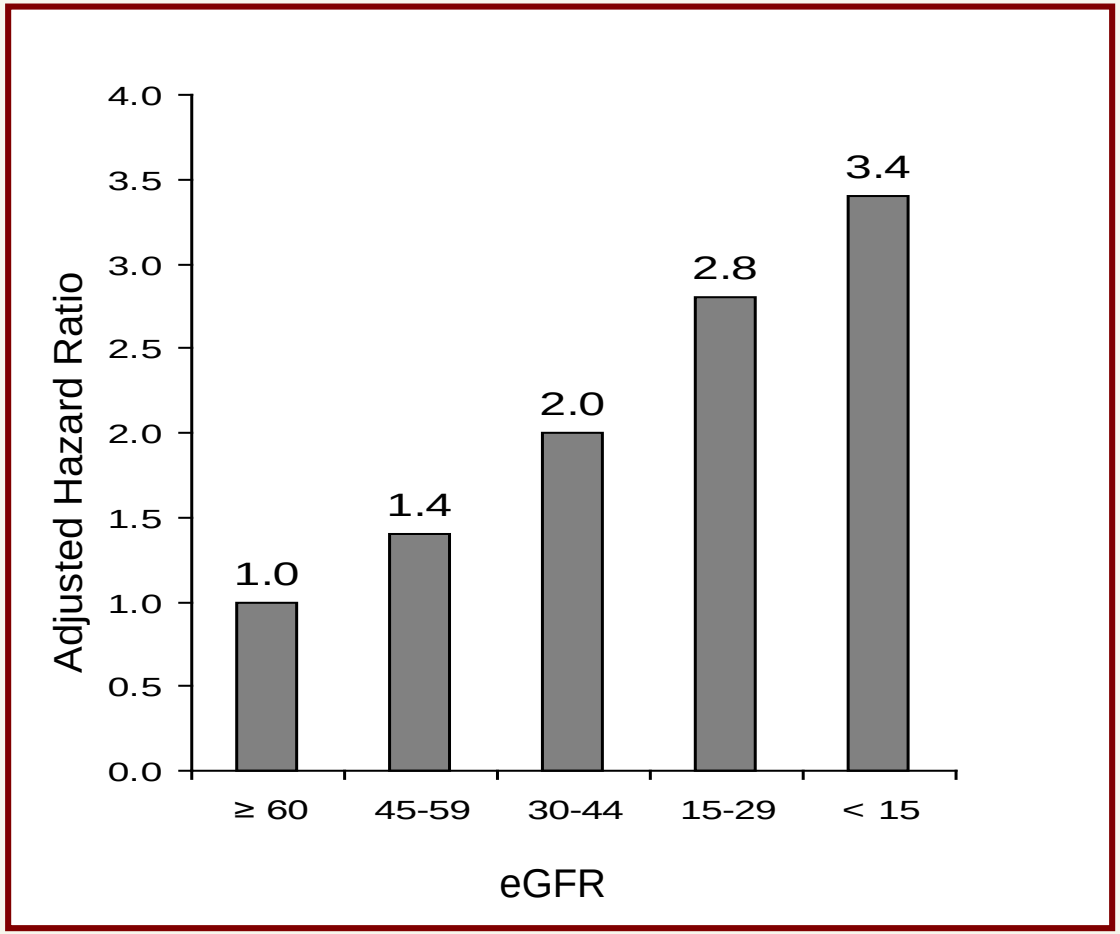
USRDS ADR, 2007

CKD is prevalent in CVD



Ix, et al., 2003; Anavekar, et al., 2004; Shlipak, et al., 2004.

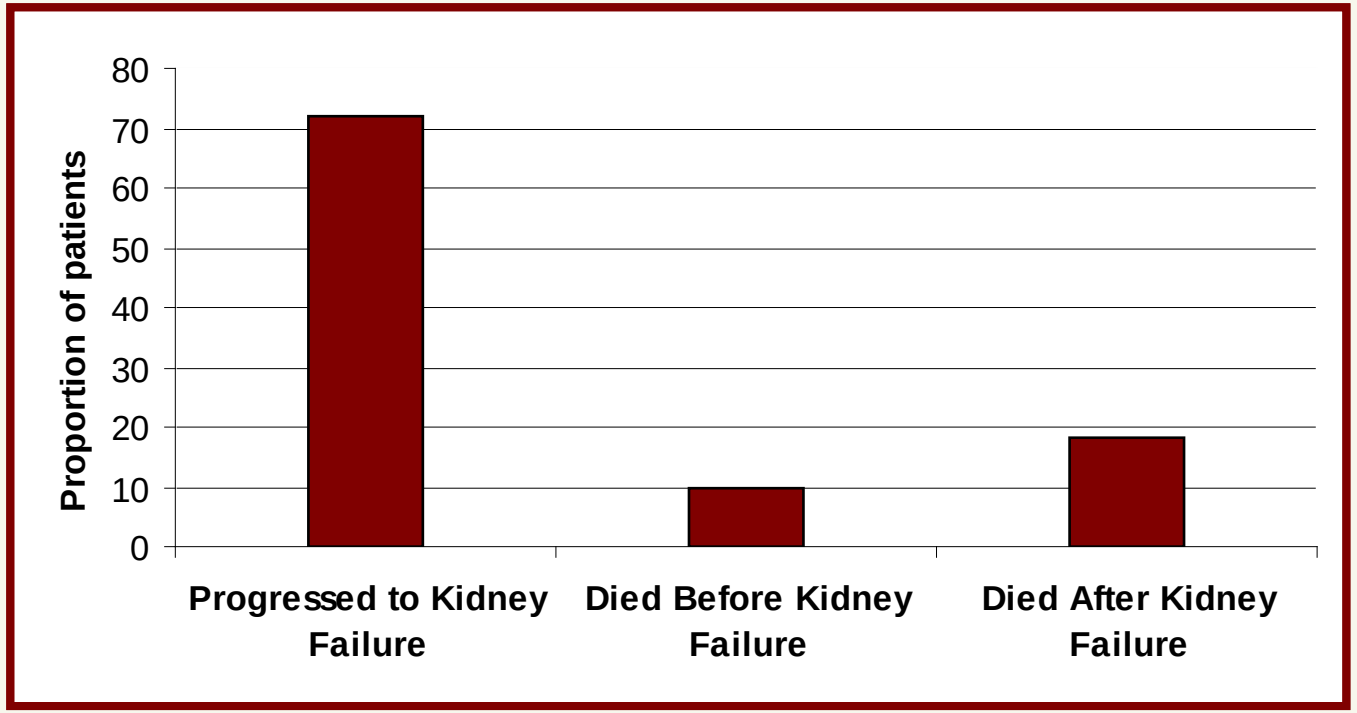
In addition to ESRD, CKD leads to CVD



Adjusted* hazard ratio for CVD events

Go, et al., 2004

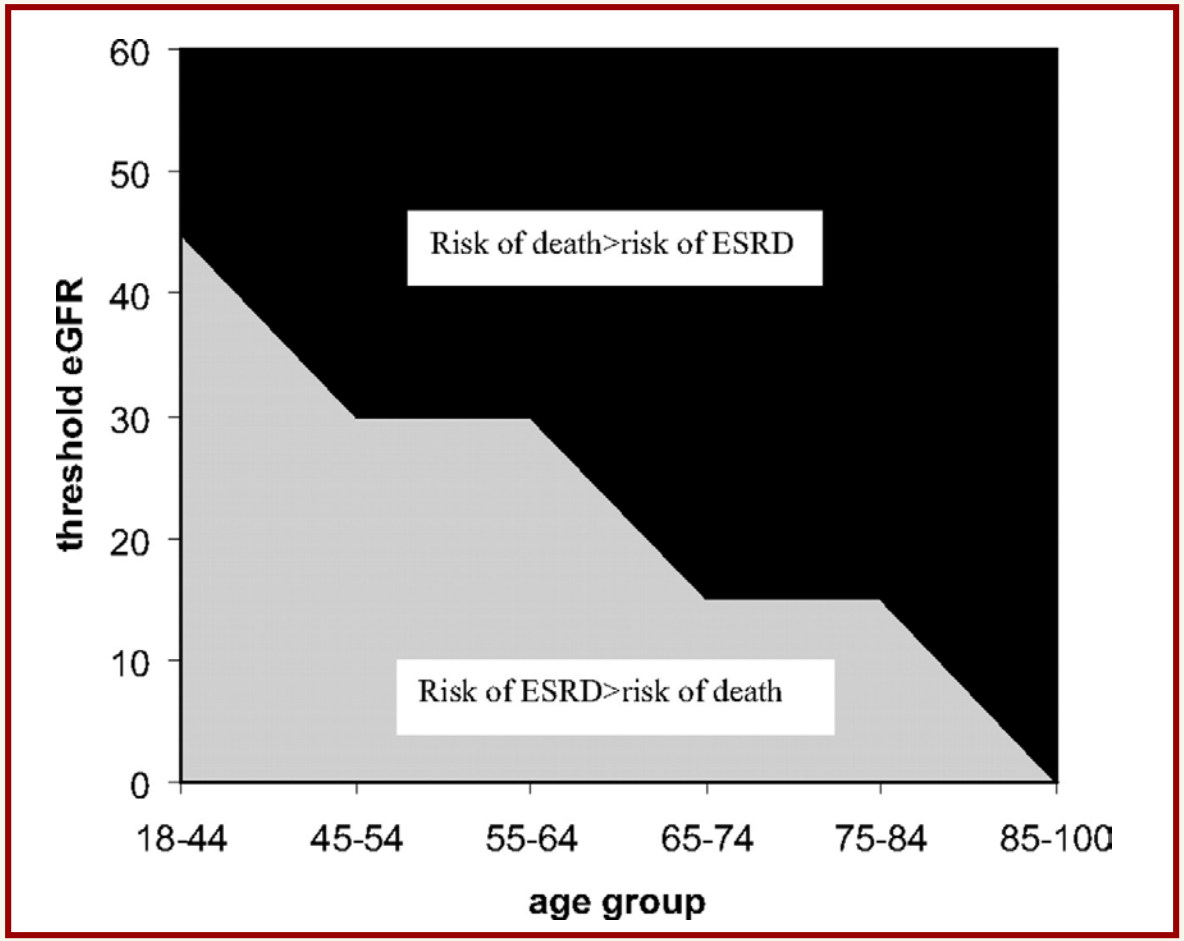
People with CKD do progress to kidney failure–especially those middle-aged and younger



Long term (7 year) follow up of 408 non-diabetic CKD patients
(mean initial GFR=39, mean initial age=52 year old)

Levey, et al., 2006

Younger people with CKD are more likely to develop ESRD before death



Annual mortality by age group and eGFR.

O'Hare, 2006

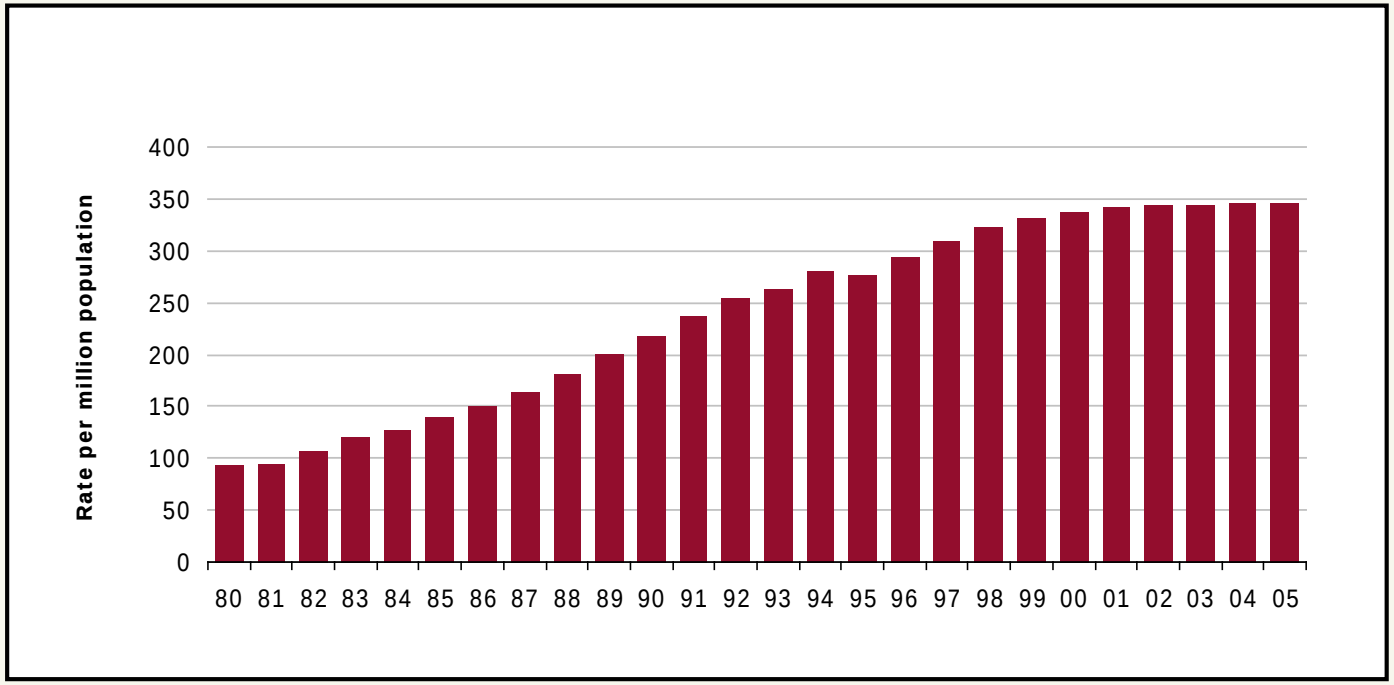
We can have an impact on progression of CKD

- Intensive glycemic control lessens progression from microalbuminuria in Type 1 diabetes–goal in Type 2 is less clear
  - DCCT, 1993
  - ACCORD, 2008

- Antihypertensive therapy with ACE Inhibitors or ARBs lessens proteinuria and progression
  - Giatras, et al., 1997
  - Psait, et al., 2000
  - Jafar, et al., 2001

- Blood pressure below 130/80 is beneficial
  - Sarnak, et al., 2005

Incidence of ESRD has leveled off, perhaps because of better use of preventive measures



Incident ESRD patients; rates adjusted for age, gender & race.

USRDS ADR, 2007

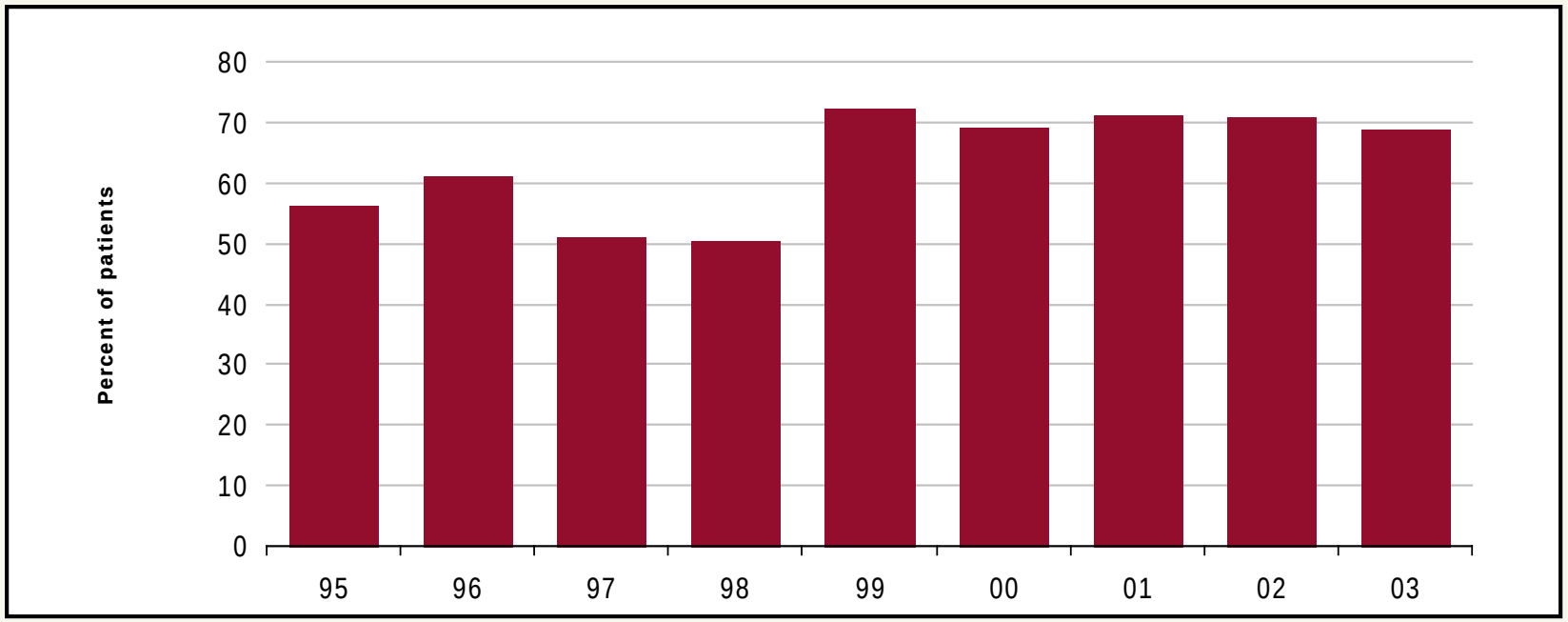
CKD is still not being identified

- Estimated GFR reporting is not universal
  - Only 38% of labs routinely report eGFR with creatinine
- CKD is usually not coded as a diagnosis
  - Less than 40% of patients with eGFR <30 were coded

Stevens, et al., 2005; NKDEP, 2008

Adherence to treatment guidelines – room for improvement

The percentage of diabetic CKD patients receiving ACE-Is/ARBs has been slow to improve



USRDS ADR, 2007

The people to test are those at greatest risk

- Diabetes mellitus
- Hypertension
- Cardiovascular disease
- Family members of patients with ESRD

Note on pediatric patients:

- CKD may start with childhood obesity
- No recommendations for routine testing

CKD is less common in children but there are risk factors

- Family history of polycystic kidney disease or other genetic kidney disease
- Renal dysplasia or hypoplasia
- Urologic disorders—especially obstructive uropathies

Hogg, et al., 2003

2 simple tests will identify CKD in adults

- **eGFR -** Estimated GFR from serum creatinine using the MDRD equation

- **UACR -** Urine albumin to creatinine ratio on a “spot” urine sample
    - 24-hour urine collections are NOT needed

- Diabetics should be tested once a year. Others at risk can be tested less frequently as long as normal.

The perils of using serum creatinine to "guess" level of renal function

	24-yo Black Man	63-yo White Man	59-yo White Woman
SCr	1.3 mg/dL	1.3 mg/dL	1.3 mg/dL
GFR as estimated by MDRD Study equation	≥60 mL/min/1.73 m^2	59 mL/min/1.73 m^2	45 mL/min/1.73 m^2

Automatic eGFR by the laboratory reporting is best

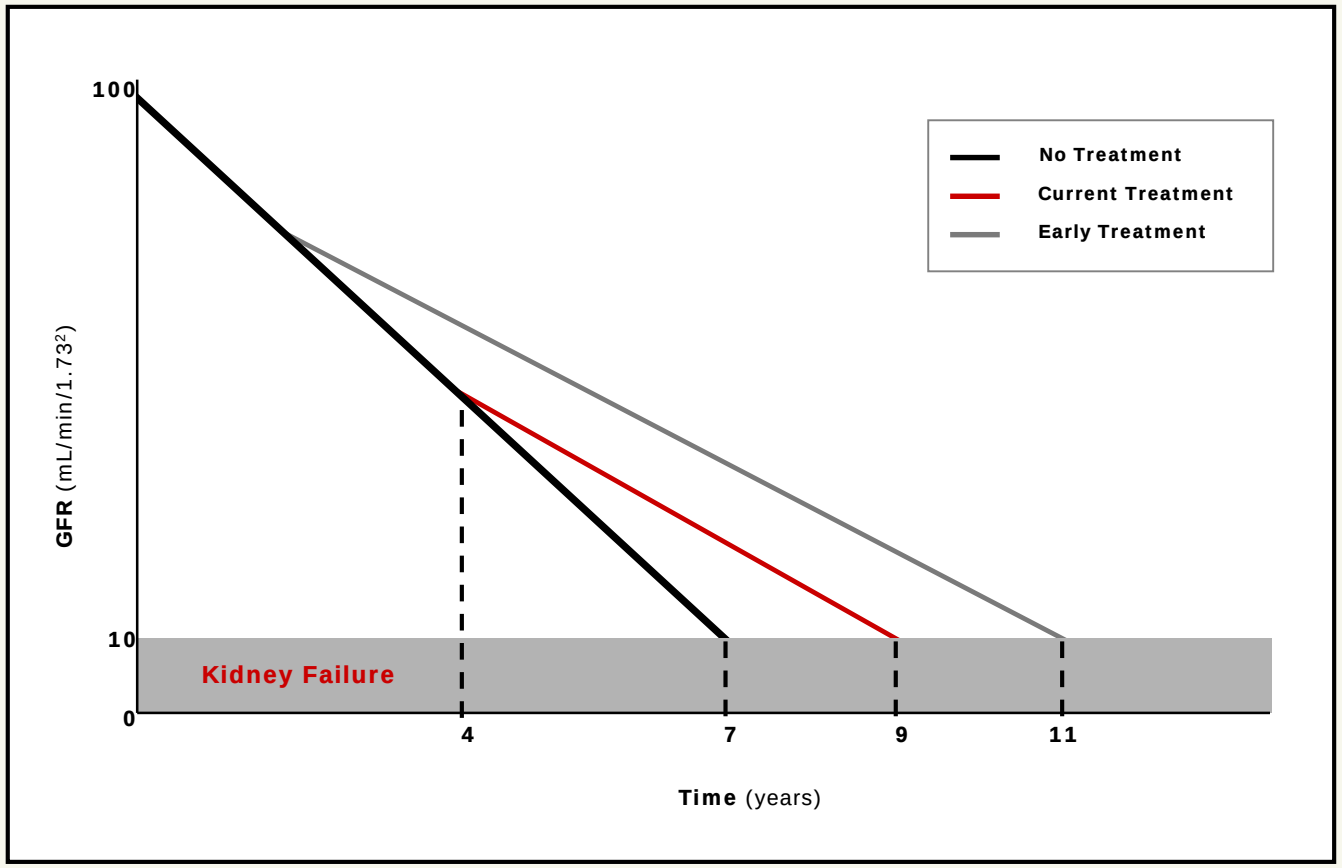
- GFR is the accepted measure of kidney function
- GFR is difficult to infer from serum creatinine alone
- Automatic reporting identifies CKD patients with apparently “normal” serum creatinine
  - Reduces barrier to early detection and identifies people at high risk for contrast agents and other nephrotoxins

Caveats to eGFR

- An estimate based on population data--not the patient's *actual* GFR

- Not reliable when used with patients:
  - with GFR above 60 ml/ min/1.73 m^2
  - with rapidly changing creatinine levels (e.g., acute renal failure in the ICU)
  - with extremes in muscle mass, e.g. cachexia or paraplegia
  - under age 18

Early treatment can make a difference



What can primary care providers do?

- Recognize and test at-risk patients
- Educate patients about CKD and treatment
- Focus on good glycemic control in people with diabetes
- For those with CKD:
  - Blood pressure below 130/80
  - Use an ACE inhibitor or ARB
  - More than one drug is usually required
  - A diuretic should be part of the regimen

What can primary care providers do? (Continued)

- Monitor eGFR and UACR
- Treat cardiovascular risk, especially with smokers and hypercholesterolemia
- Screen for anemia (Hgb), malnutrition (albumin), metabolic bone disease (Ca, Phos, PTH)
- Refer to dietitian for nutritional guidance
- Consult or team with a nephrologist
- Encourage labs to report estimated eGFR and urine albumin/creatinine ratios

Nephrology referral suggestions

- To assist with diagnostic challenge (e.g. decision to biopsy)
- To assist with therapeutic challenge (e.g. blood pressure)
- Rapid decay of estimated GFR
- Most primary kidney diseases, (e.g. glomerulonephridites)
- Preparation for renal replacement therapy, especially when GFR less than 30

Nephrology referral suggestions, cont.

- Regardless of when you refer:
  - Obtaining preliminary evaluation (e.g. ultrasound, screening serologies)
  - Providing consultant with patient history including serial measures of renal function

Primary care providers – First line of defense against CKD

- Primary care professionals can play a significant role in early diagnosis, treatment, and patient education
- Therapeutic interventions for diabetic CKD are similar to those required for optimal diabetes care
    - Control of glucose, blood pressure, and lipids
- A greater emphasis on detecting CKD, and managing it prior to referral, can improve patient outcomes

CKD is Part of Primary Care

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Nephrology

- Renal function
  - AKI
  - CKD
  - Renal replacement therapy
- Medication adjustment in renal impairment
- Hypertension
  - Likely highest contributor to CKD in Malawi
  - Adjustment needed depending on fluid balance / AKI
- Volume status and pulmonary edema

Renal replacement therapy

- Hemodialysis / peritoneal dialysis
- Indications: AEIOU, ESRD with symptoms
  - Acidosis
  - Electrolyte imbalance
  - Ingestions (poisons) of dialyzable toxins
  - Oxygenation / Other (volume status/pulmonary edema, hyperthermia)
  - Uremia (symptomatic)
- Logistics: catheter insertion (or AV fistula), transport to dialysis center or ICU
- Chronic renal replacement therapy: expensive, high complications and morbidity & mortality
- Risk vs benefits – short term better than long term (chronic renal replacement therapy not feasible for most Malawians)

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Medication adjustment

- Medication adjustment in CKD
  - Based on eGFR
  - Adjustment of chronic doses CKD progression versus AKI on CKD
  - Most common errors? -> metformin, antibiotics, avoidance of **INIDICATED** meds
- Medication adjustment in AKI
  - eGFR not accurate (guess based on UOP and lab trends)
    - What happens to labs after surgical nephrectomy?
  - Avoid both nephrotoxic antibiotics and renally cleared medications with narrow therapeutic window (gentamicin, digoxin, high dose insulin)
  - Hold confounding drugs (ACE-I/ARB, NSAIDs)
  - Complex (require specialist input) -> HDU/ICU cases (stroke, HTN emergency, MI sepsis, complex malaria), ARVs/TB, acid-base disturbance

Medication adjustment

- Step 1: calculate eGFR
  - ALL patients with AKI or CKD (creatinine > 1.5 mg/dL)
  - ALL patients > 55 years old
  - ALL patients with oliguria
  - ALL HDU/ICU patients
- Step 2: look up medication adjustments
  - BOTH home meds and drugs you are initiating
  - Need adjustment – most antibiotics/ARVs/TB, insulin, most oral diabetic meds, some anti-hypertensives, DOACs, antiepileptic drugs
- Step 3: follow renal function to re-adjust
  - Daily U&E until plateau
- Step 4: Establish AKI versus CKD
  - Inform patients/guardians
  - Written instructions on medications to avoid
  - RESUME outpatient medications once AKI resolves

Nephrology

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Hypertension and Its Treatment

A European Approach

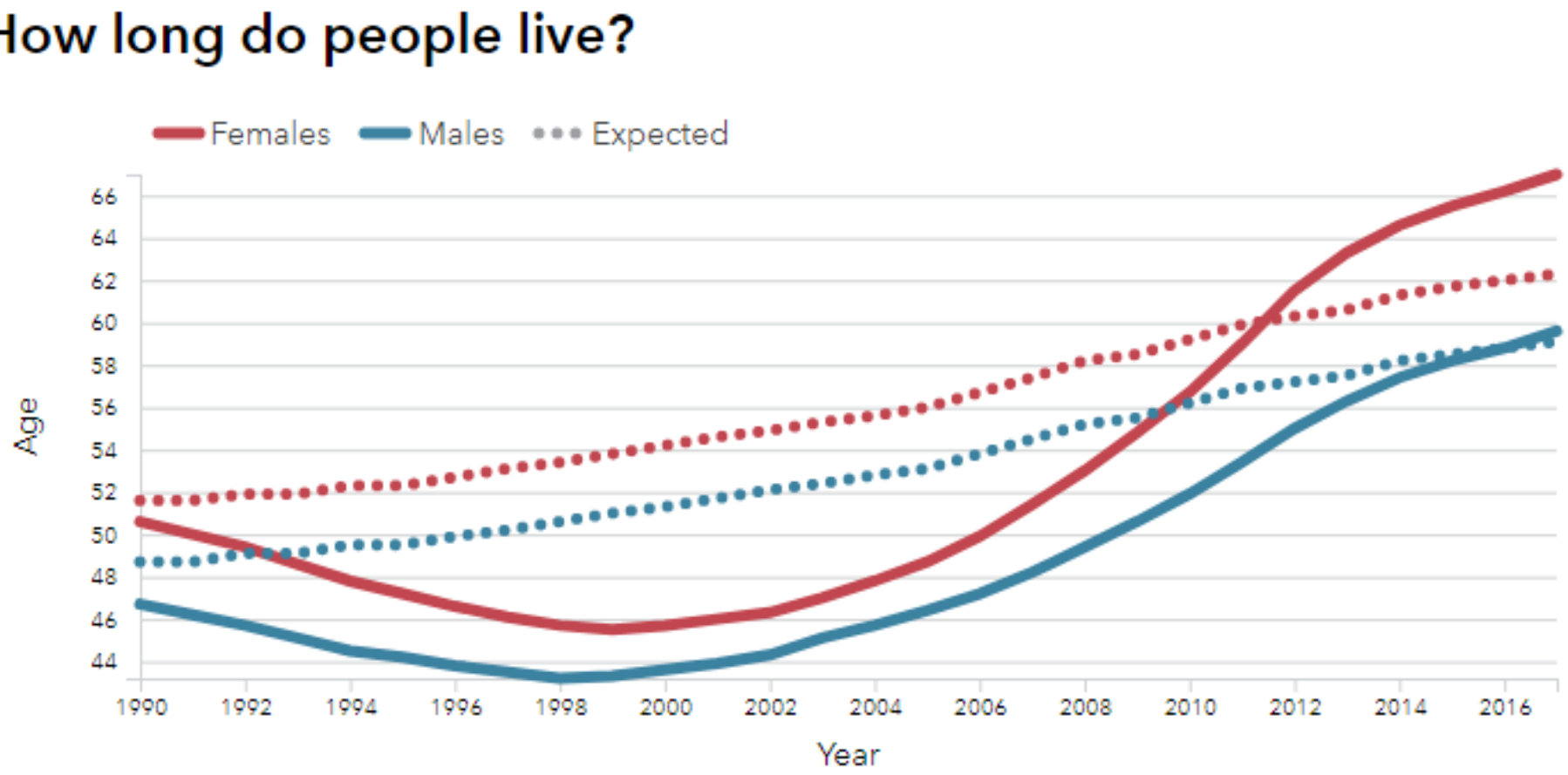
Preston Seaberg, M.D.

Edited and supervised by Dr. Tiffany Priester

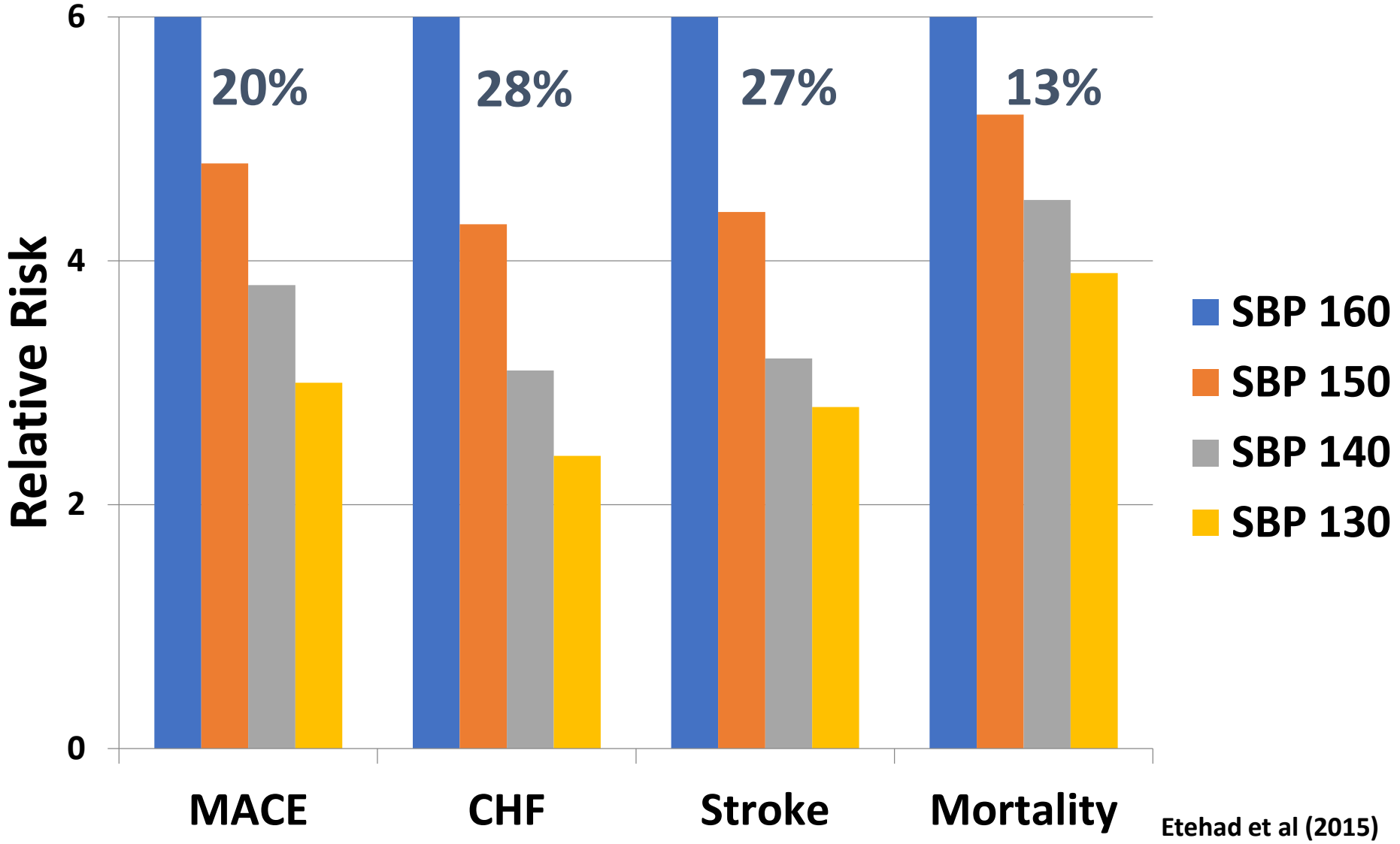
Learning Objectives

- **Diagnose and evaluate a person with hypertension**
- **Treat a person with hypertension**
- **Prevent complications of hypertension and its treatment**

Life Expectancy in Malawi



BP Control Reduces Risk



Etehad et al (2015)

Hypertension (HTN): Definition, Diagnosis

- **High normal: 130-139/80-89**
- **Hypertension: ≥140/90**
- **≥2 readings, separated in time***

HTN: Definitions

Classification of office blood pressure[a] and definitions of hypertension grade[b]

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension[b]	≥140	and	<90

BP = blood pressure; SBP = systolic blood pressure.

HTN: Special Definitions

- **Pregnancy: same definitions**
  - **Pre-existing: onset prior to 20 wk gestation**
  - **Gestational: onset ≥20 wk gestation**
  - **Pre-existing + gestational**
  - **Pre-eclampsia: gestational HTN w/ proteinuria > 300 mg/24 h**
  - **Antenatally unclassifiable HTN**

HTN: Evaluation

- **Identify cardiovascular risk factors**
- **Briefly screen for secondary causes**
- **Assess for target-organ damage**

HTN: Risk Assessment

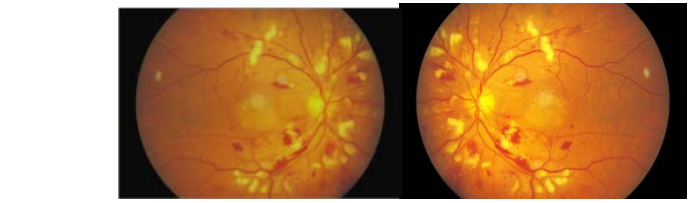
- Coronary artery disease
- Peripheral arterial disease
- Cerebrovascular disease
- Chronic kidney disease
- Diabetes mellitus
- **Obstructive sleep apnea**
- **Preeclampsia**
- **Smoking**
- **Sedentary lifestyle**

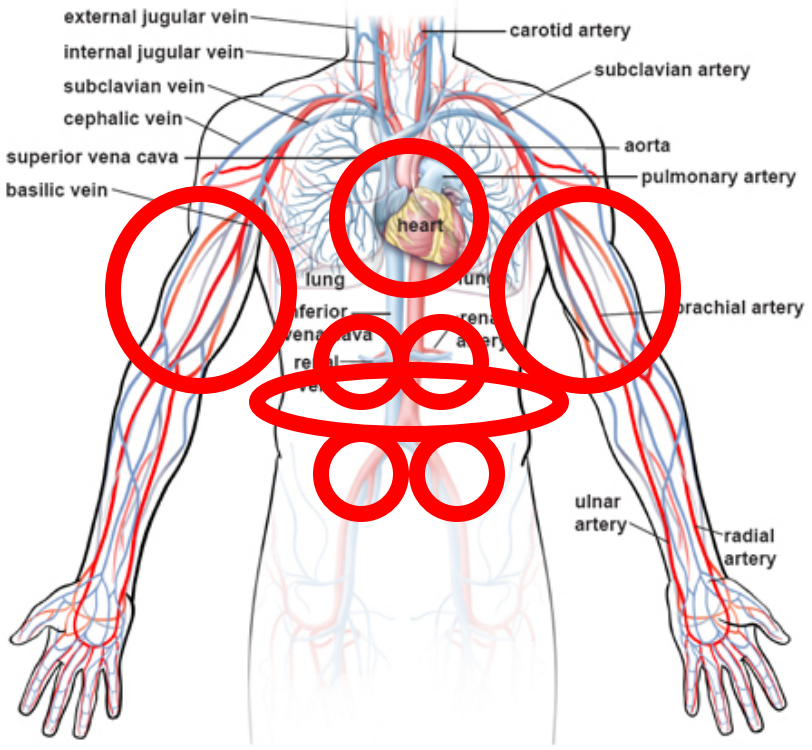
HTN Evaluation: History

- **Smoking**
- **Physical activity**
- **Diet, particularly sodium**
- **Family history**
- **Alarming symptoms**

HTN Evaluation: Physical Exam

- **Check BP in both arms**
- **Funduscopic exam**
- **BMI and waist circumference**
- **Heart**
- **Vessels**





HTN Evaluation: Testing

- Urea, creatinine and electrolytes
- Urinalysis
- Fasting glucose
- Glycohemoglobin
- Fasting cholesterol profile
- Hematocrit (full blood count)
- Electrocardiogram
- Thyroid stimulating hormone

Routine annual follow-up tests in blue

HTN: Diagnosis, Evaluation Summary

- **Check BP of all adults, each office visit**
- **Be alert when BP ≥ 130/80**
- **Diagnose when BP ≥ 140/90**
- **Confirm readings over time***
- **Standard assessment when diagnosed**
  - **History and physical exam**
  - **Laboratory tests**
  - **ECG**

Treat hypertension

Choose whom and when to treat

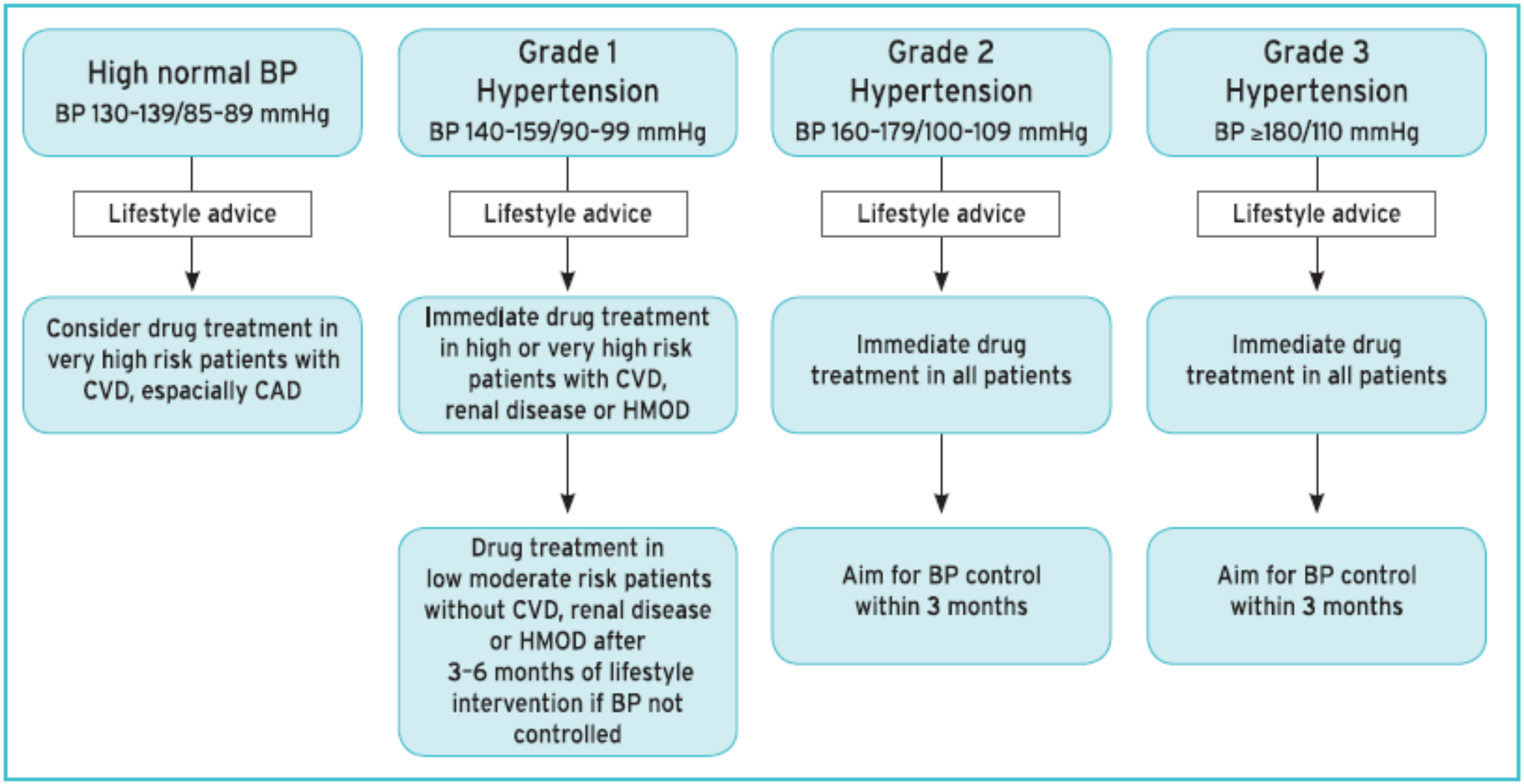
Counsel on effective lifestyle modification

Select medication(s) based on comorbidities

Set treatment target

Troubleshoot suboptimal treatment response

HTN Treatment: Who and When?



HTN Treatment: How About Pregnancy?

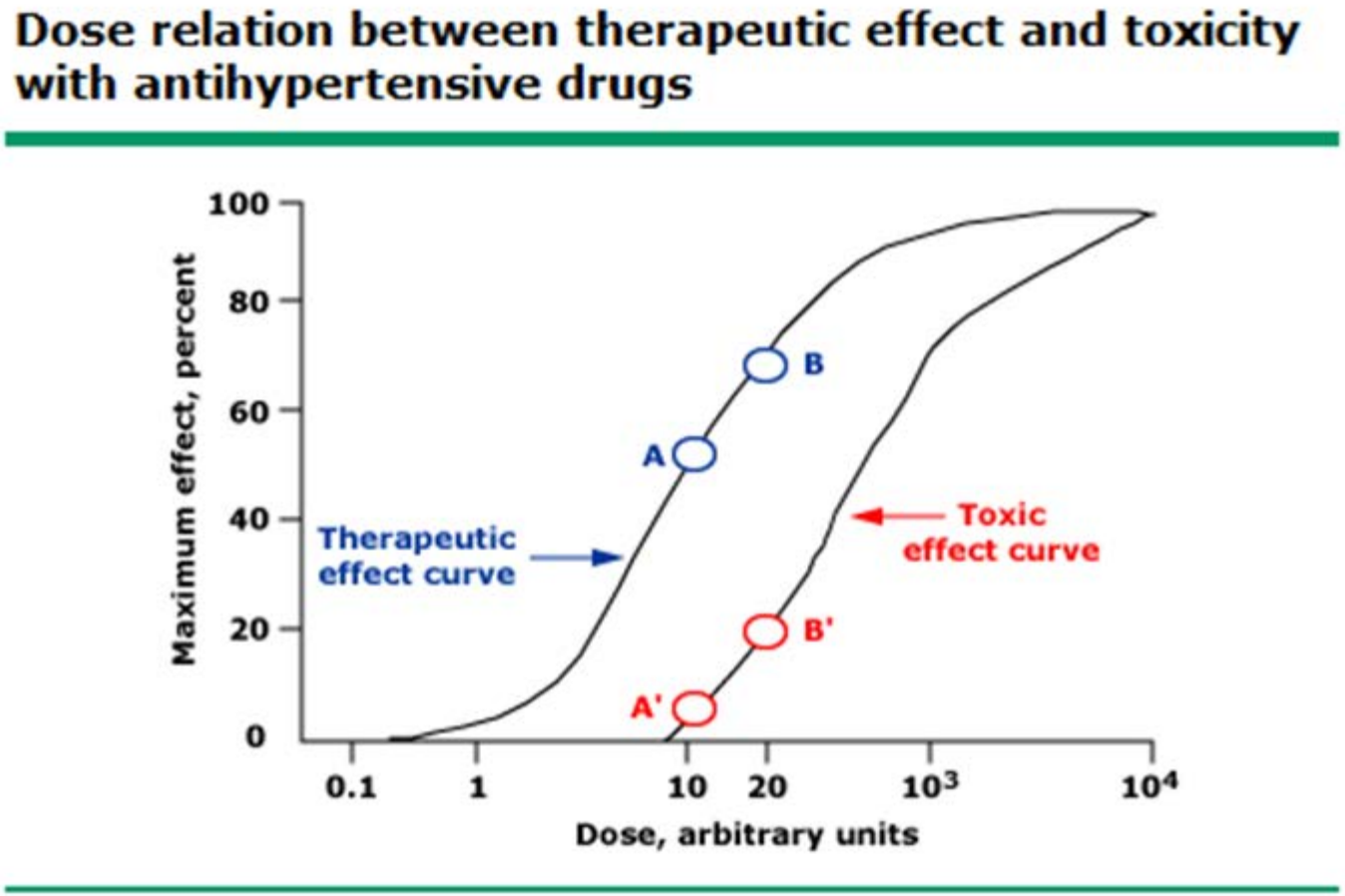
- **All women w/ BP ≥150/95mmHg;**
- **Gestational hypertension BP > 140/90**
- **Pre-existing HTN + gestational HTN > 140/90**

HTN: Effective Lifestyle Modifications

- **Alcohol moderation**
- **Smoking cessation**
- **Salt restriction**
- **DASH diet**
- **Get to ideal body weight**
- **Regular physical activity**

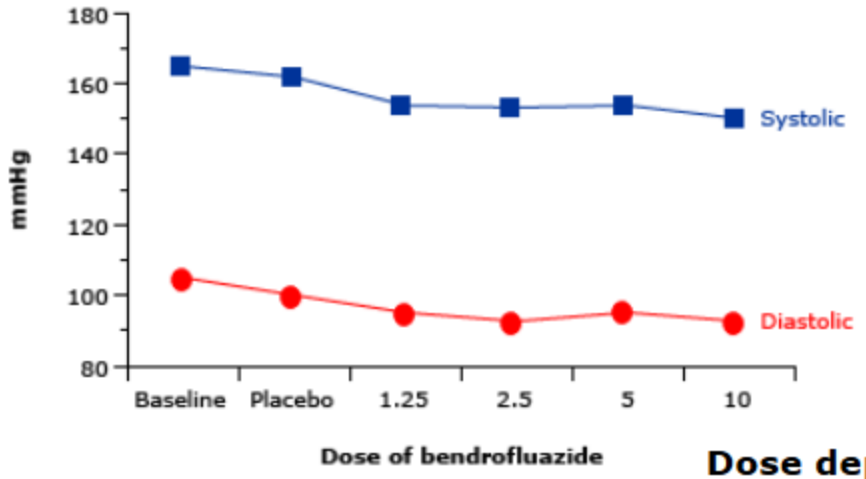
HTN: DASH Diet

HTN Medications: First Things First

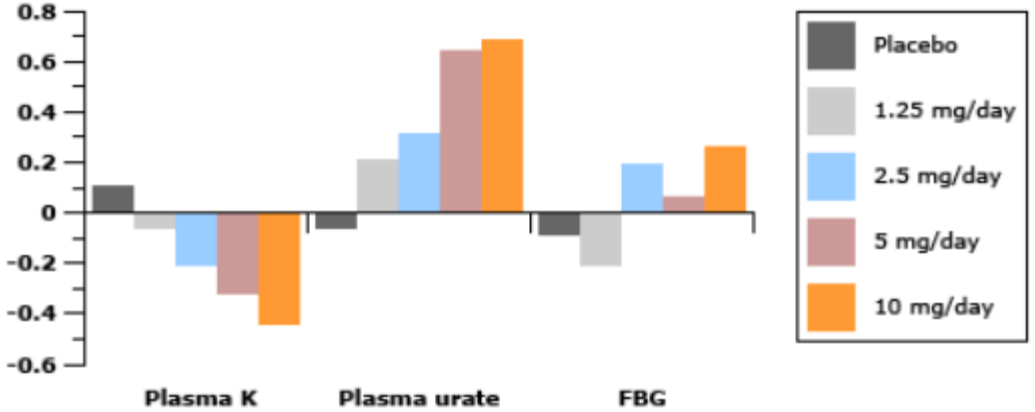


HTN Medications: First Things First

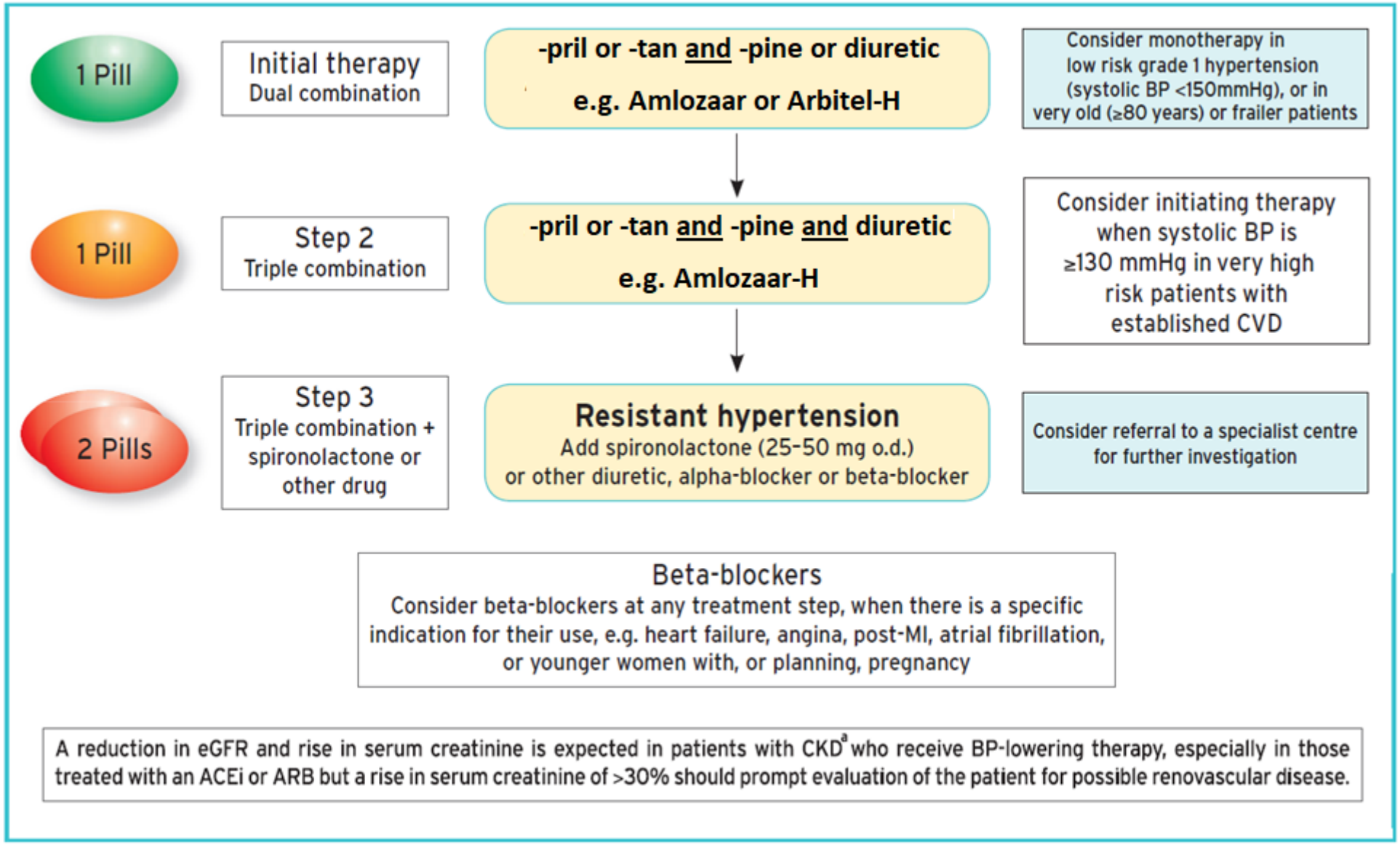
Antihypertensive dose response to thiazide therapy



Dose dependence of thiazide-induced side effects



Summary: Treatment



HTN Medications: Rx by Comorbidity

- **Coronary disease: enalapril or losartan, bisoprolol, atenolol**
- **Stroke: enalapril or losartan, hydrochlorothiazide**
- **Heart failure: enalapril or losartan, carvedilol, (maybe frusemide), (maybe spironolactone),**
- **Kidney disease: enalapril or losartan**
- **Atrial fibrillation: bisoprolol, atenolol, enalapril or losartan**

HTN: Treatment Targets

- **First objective: <140/90**
- **Once there: may try even harder!**
  - **Patients < 65: SBP 120-129***
  - **Patients 65-80: SBP 130-139***
  - **Patients > 80: SBP 130-139****
- **DBP target < 80 mm Hg for all**

HTN: Lack of Treatment Response

- **Physician inertia**
- **Insufficient combo therapy**
- **Treatment complexity**
- **Patient adherence**
- **Secondary causes**

- **90-95% of patients can achieve target**

HTN: Resistant Hypertension

- **BP > goal on ≥3 drugs (including diuretic)**
- **1. Exclude nonadherence, iatrogenesis**
- **2. Consider secondary causes (5-10% of HTN)**
- **3. Add spironolactone 25-50 mg OD**

  or
- **Add bisoprolol or nitrate/hydralazine**
- **4 .Refer to internist**
  - **Advanced Rx strategies: change diuretics**

Prevent complications

Prevent and treat complications and comorbidities

Mitigate adverse effects of medications

HTN: Prevention of Complications

- **Yearly Screening**
  - **Urea, creatinine and electrolytes**
  - **Urinalysis**
  - **Glycohemoglobin**
  - **Fasting cholesterol profile**
  - **Hematocrit (full blood count)**
- **Statin**
  - **Diabetes**
  - **Coronary or cerebrovascular disease**
- **Aspirin**
  - **Coronary or cerebrovascular disease**

HTN: Complications of Therapy

Table 20 Compelling and possible contraindications to the use of specific antihypertensive drugs

Drug	Contraindications	
	Compelling	Possible
Diuretics (thiazides/thiazide-like, e.g. chlorthalidone and indapamide)	• Gout	• Metabolic syndrome • Glucose intolerance • Pregnancy • Hypercalcaemia • Hypokalaemia
Beta-blockers	• Asthma • Any high-grade sinoatrial or atrioventricular block • Bradycardia (heart rate <60 beats per min)	• Metabolic syndrome • Glucose intolerance • Athletes and physically active patients
Calcium antagonists (dihydropyridines)		• Tachyarrhythmia • Heart failure (HFrEF, class III or IV) • Pre-existing severe leg oedema
Calcium antagonists (verapamil, diltiazem)	• Any high-grade sinoatrial or atrioventricular block • Severe LV dysfunction (LV ejection fraction <40%) • Bradycardia (heart rate <60 beats per min)	• Constipation
ACE inhibitors	• Pregnancy • Previous angioneurotic oedema • Hyperkalaemia (potassium >5.5 mmol/L) • Bilateral renal artery stenosis	• Women of child-bearing potential without reliable contraception
ARBs	• Pregnancy • Hyperkalaemia (potassium >5.5 mmol/L) • Bilateral renal artery stenosis	• Women of child-bearing potential without reliable contraception

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; HFrEF = heart failure with reduced ejection fraction; LV = left ventricular.

Annual hypertension template Syhos

References

- Williams B et al (2018). European Heart Journal: 39, 3021-3104
- Ettehad D et al (2015). Lancet: 387;10022. pp957-967.
- http://www.healthdata.org/malawi

Nephrology

- Renal function
  - AKI
  - CKD
  - Renal replacement therapy
- Medication adjustment in renal impairment
- Hypertension
  - Likely highest contributor to CKD in Malawi
  - Adjustment needed depending on fluid balance / AKI
- Volume status and pulmonary edema

Nephrology – volume status

- Normally urine output (UOP) slightly less than oral intake
  - Insensitive losses
- Technicality
  - Dehydration (elevated plasma sodium, reduced free water)
  - Intravascular volume (hypovolemia, hypervolemia)
  - Total body water (third spacing)
- Complex vascular-hepato-cardio-renal-endothelial interaction
  - CCF, cirrhosis, ARDS, post-surgical third spacing
  - Hepato-renal syndrome (often eGFR improves with tap + spironolactone)
  - Cardio-renal syndrome (often eGFR improves with diuresis)

Volume status

- Intravascular volume and total body water
  - Acute DKA and acute shock (both IVV and TBW down)
  - Decompensated CCF (both IVV and TBW up)
  - Malnutrition (IVV down but TBW up)
  - Resuscitated shock and MODS (IVV ↑↓ but TBW up)
- Goal – maintain adequate perfusion to vital organs
- Compromise – third spacing can lead to anasarca or intubation
- Race analogy – which pathology “wins” the race?
  - Reversal of underlying pathophysiologic state before fatal organ failure
  - If nothing ”reverses” then may get fatal cerebral/pulmonary edema
  - If insufficient fluid resuscitation then risk fatal hypoperfusion kidneys/brain/tissues

Nephrology – volume status

- AKI
  - Initial fluid resuscitation
  - Once euvolemic -> judicious fluid replacement
  - Post AKI diuresis (can be VOLUMINOUS)
- CKD ± CCF
  - As UOP decreases, decrease PO intake to match (versus edema)
  - Lowest “reasonable” fluid restriction 500 mL / day short term and 750 mL / day long term
  - As creatinine increases, diuretic dose must increase to be effective
  - MAXIMUM diuretic dose?
  - May need “boost” with HCTZ or metolazone
  - Follow electrolytes closely
  - Use ACE-I / ARB if possible (<u>especially</u> if proteinuria or HFrEF)

Nephrology

- Renal function
  - AKI
  - CKD
  - Renal replacement therapy
- Medication adjustment in renal impairment
- Hypertension
  - Likely highest contributor to CKD in Malawi
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- Volume status and pulmonary edema

- **Not covered:** acid-base disturbances including RTAs, nephron co-transporters, efferent/afferent tubule function, types of glomerulonephritidies, drugs with primarily renal excretion, kidney stones, solitary kidney, congenital abnormalities, renovascular disease, renal tumors, renal transplant, refractory hypertension, management of ESRD (metabolic bone disease, anemias, cardiovascular disease, HTN, volume status, vascular access)

- Questions???