Chronic kidney disease

4th years

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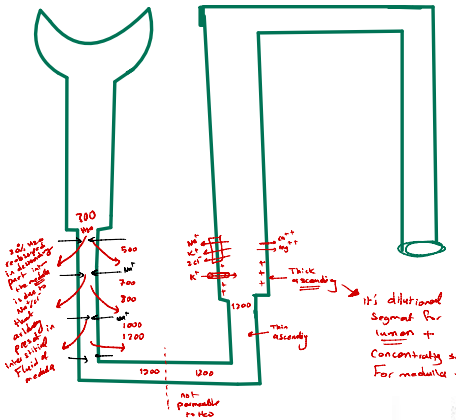
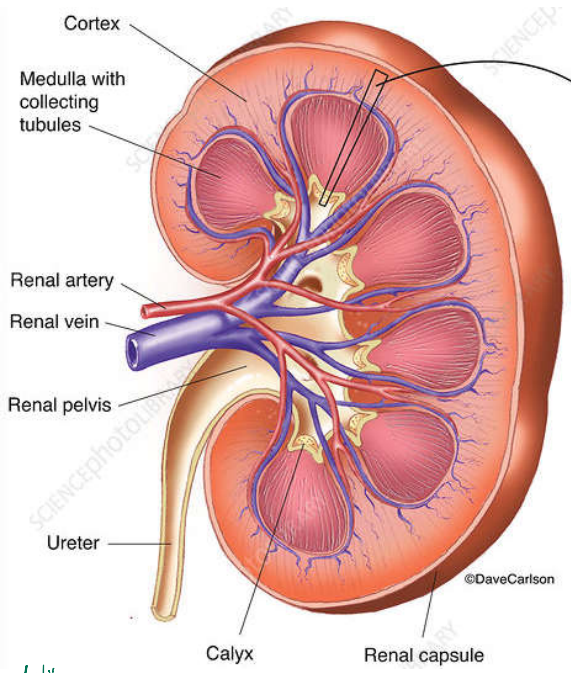
Outline

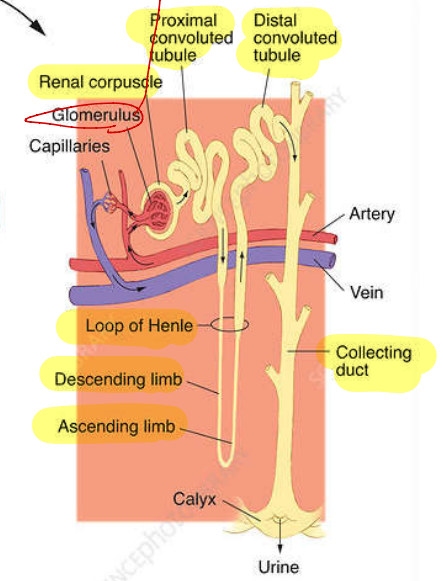
- Basics about the kidney
- Kidney functions
- GFR (estimation versus measurement)
- Pathophysiology of kidney disease
- CKD definition/ stages
- Epidemiology/Jordan
- Manifestation
- Complication
- Management (headlines)

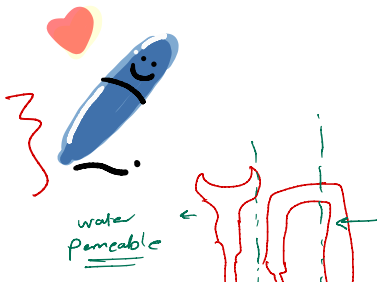
Kidney

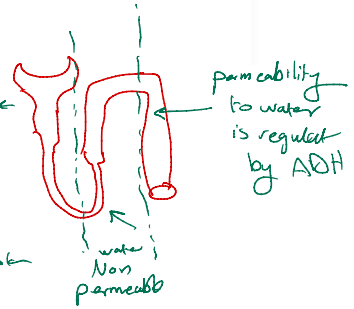
- Kidney 150 gm (heart 300 mg), 12 cm length (left kidney larger than right)
- 1.3 million nephrons each kidney (fixed number, completed early in life)
- 2 types of nephrons
- Cortical 85%: short loop of Henle
- Juxtamedullary: long loop of Henle with Vasa recta, participate in concentration of urine





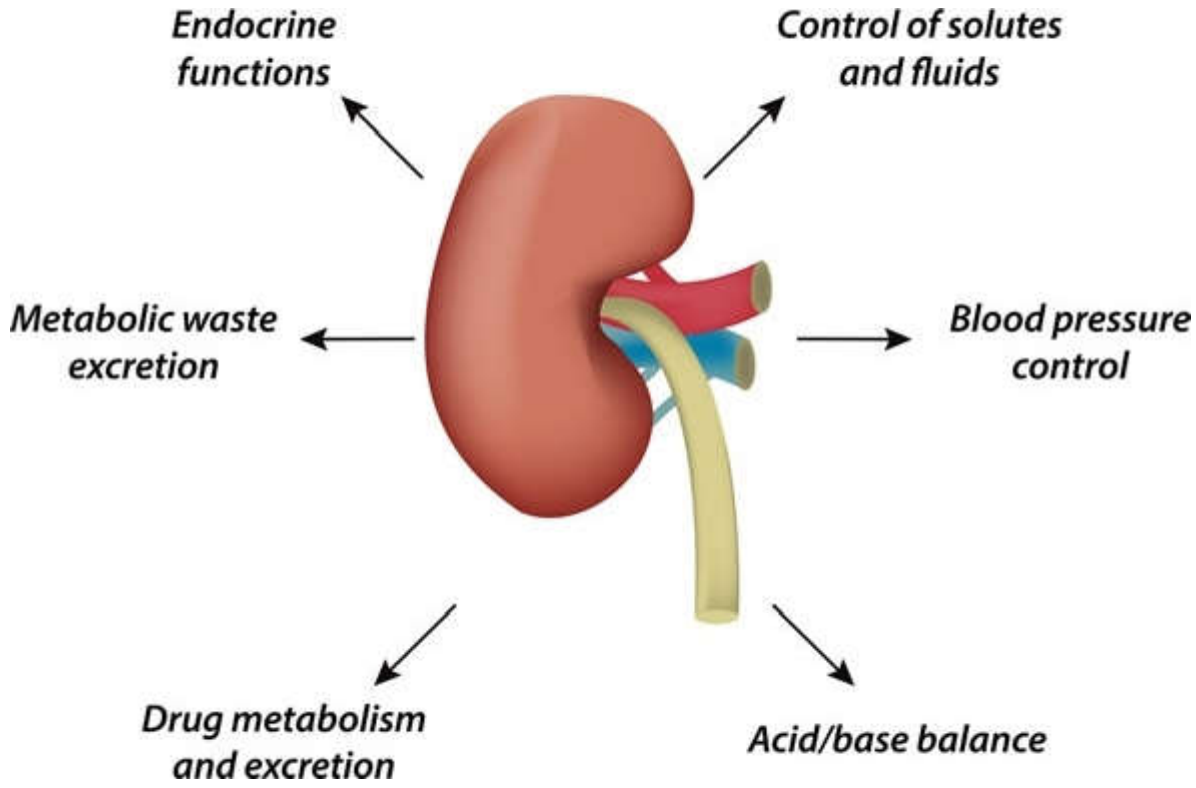






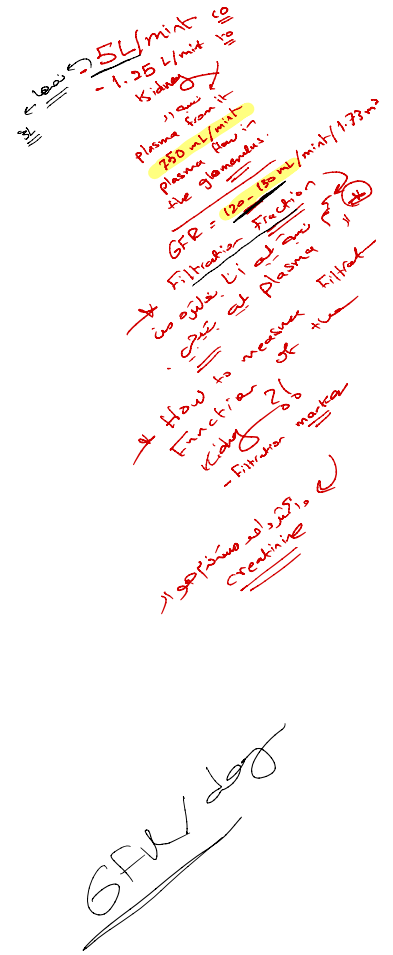
Kidney functions

- Regulation of fluid, pH, BP (short term = RAAS or long term = blood volume)
- Homeostasis of electrolytes
- Endocrine (3 hormones RAAS, activation of Vitamin D, Erythropoietin 85%) Paracrine (PG E2, NO)
- Clearance: Excretion (endogenous or exogenous waste)
- Gluconeogenesis 10% (fasting)

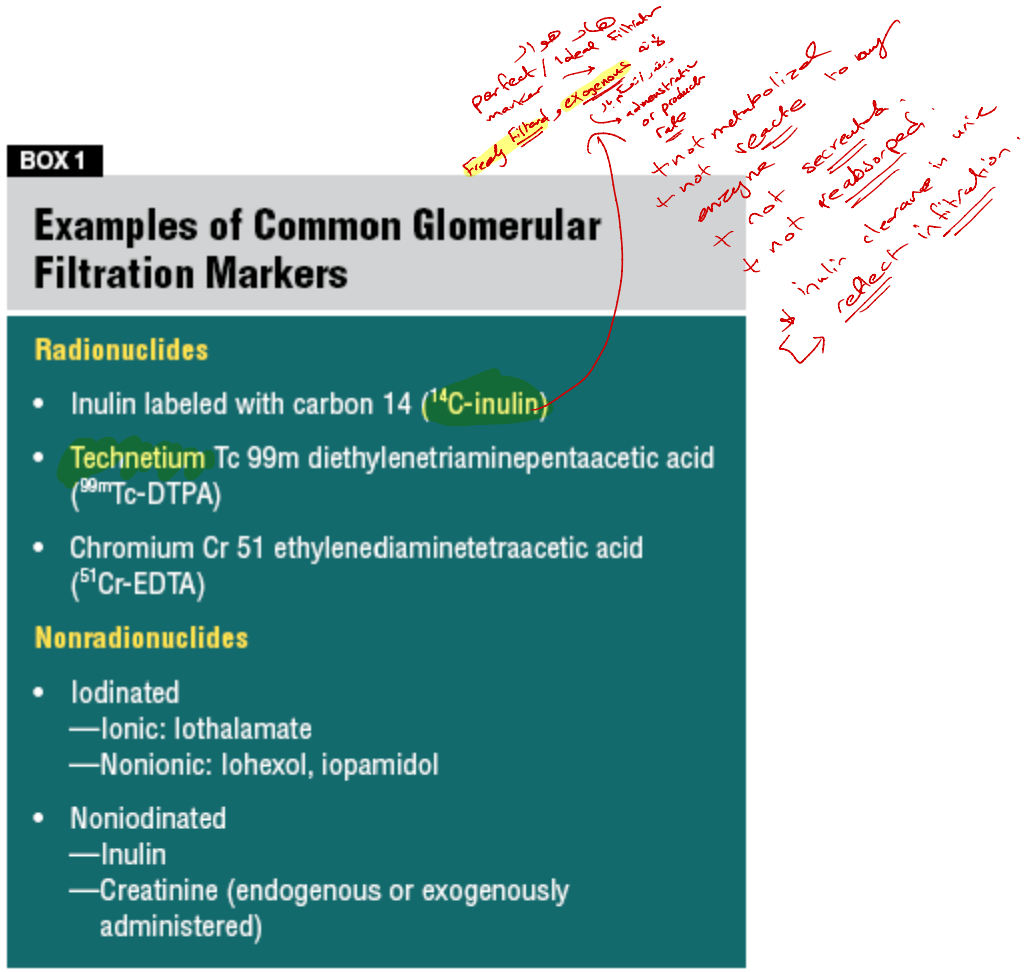


GFR (estimation versus measurement)

- Constant production ✓
- Freely filtered at the glomerulus ✓
- No tubular secretion or resorption
  - Some tubular secretion X
- No extra-renal metabolism ✓
- No extra-renal loss
  - Some GIT loss X
- Loss of creatinine through avenues other than glomerular filtration means Creatinine Clearance is slightly higher than the GFR



Other filtration marker (exogenous)



BOX 1

Examples of Common Glomerular Filtration Markers

Radionuclides

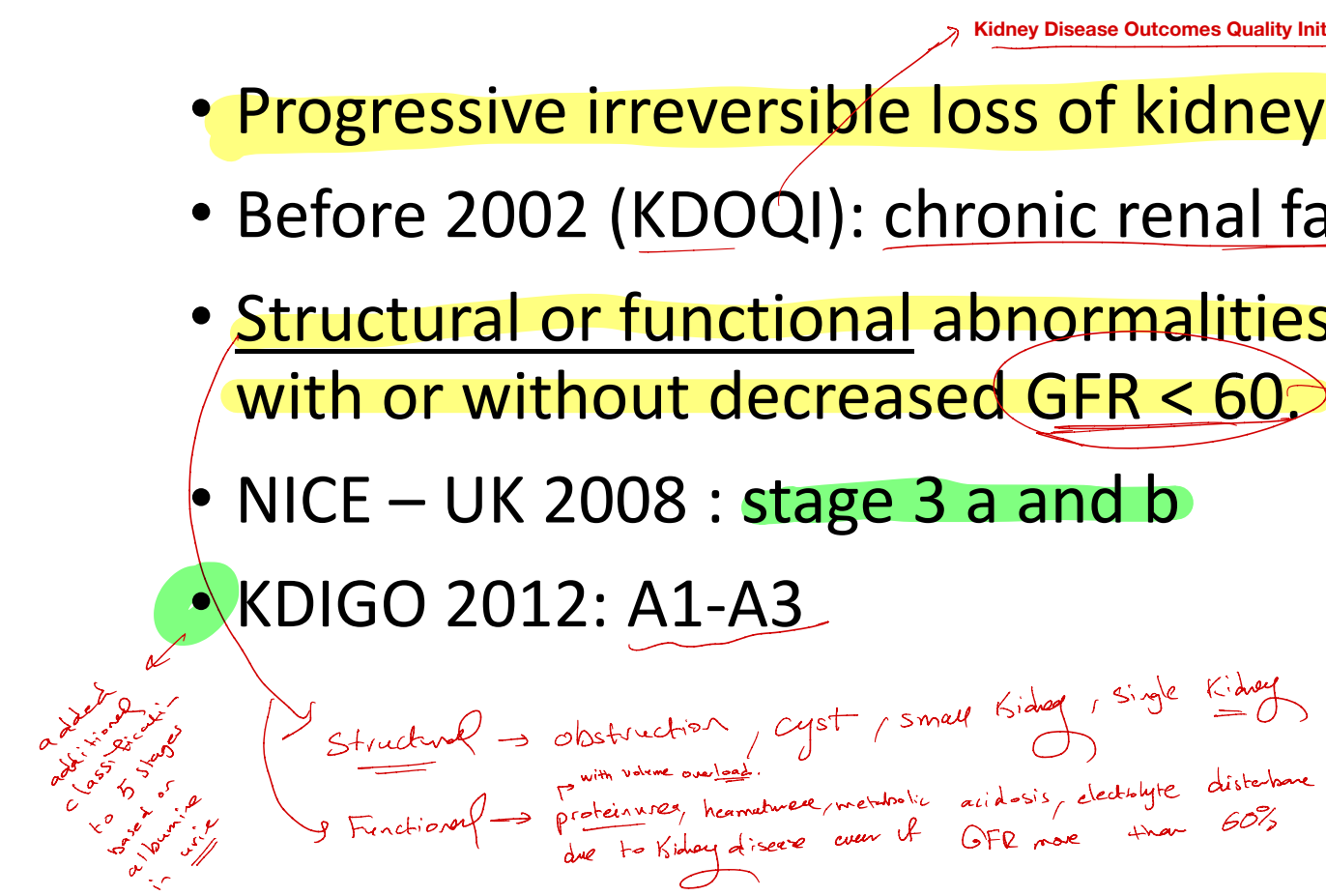
- Inulin labeled with carbon 14 (^{14}C-inulin)
- Technetium Tc 99m diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA)
- Chromium Cr 51 ethylenediaminetetraacetic acid (^{51}Cr-EDTA)

Nonradionuclides

- Iodinated
  - —Ionic: Iothalamate
  - —Nonionic: Iohexol, iopamidol
- Noniodinated
  - —Inulin
  - —Creatinine (endogenous or exogenously administered)

CKD definition

- Progressive irreversible loss of kidney functions
- Before 2002 (KDOQI): chronic renal failure
- Structural or functional abnormalities of the kidneys for >3 months, with or without decreased GFR < 60.
- NICE – UK 2008 : stage 3 a and b
- KDIGO 2012: A1-A3



Pathophysiology

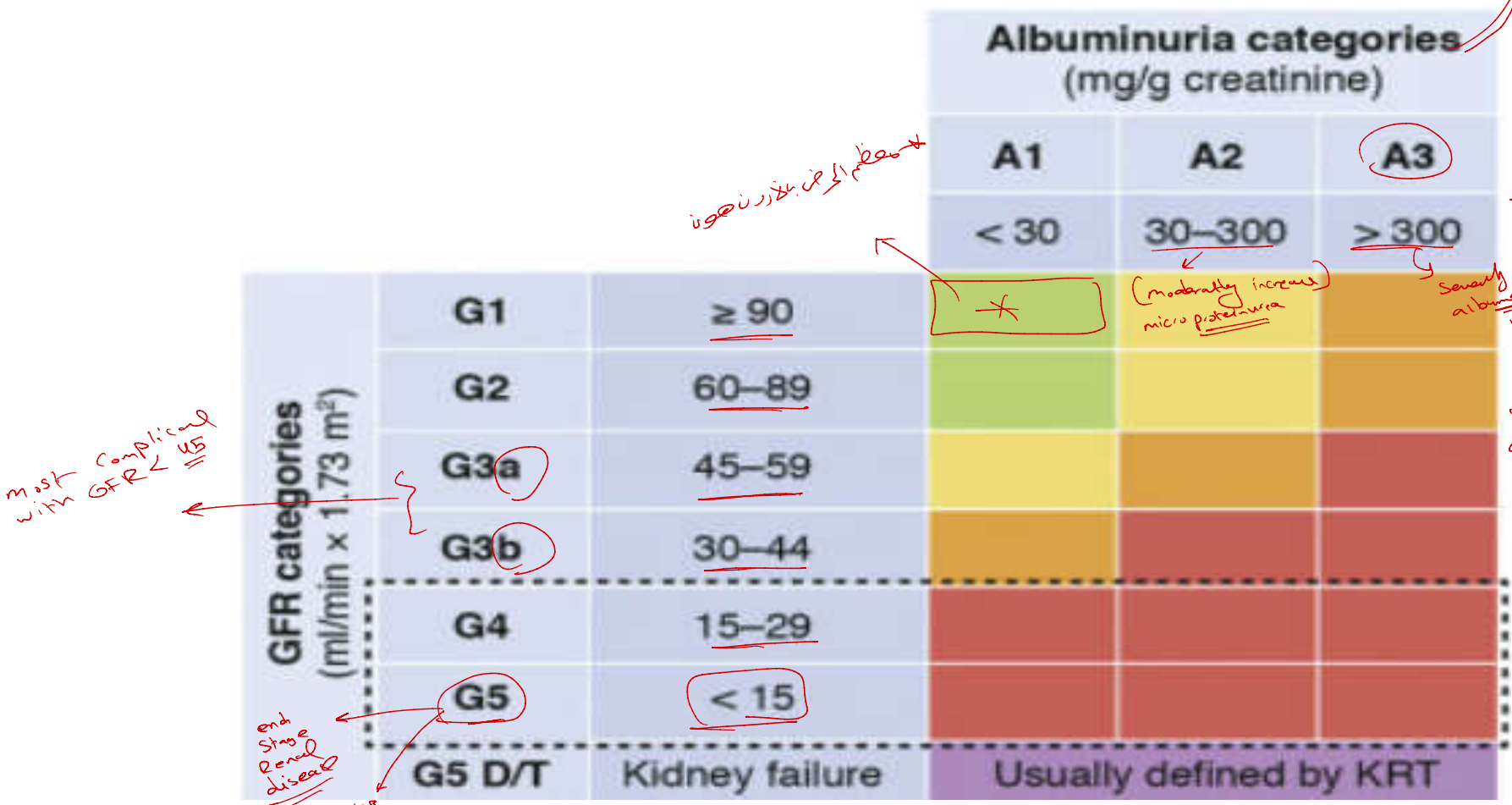
There are common pathway between different disease.

- Started by initiating injury
- Recruit inflammatory cell
- Release growth factor (balance between good and bad)
- Metalloproteinase, PA (cut the collagen)
- RAAS system activation: Ag II pro fibrotic

Transforming Factor

+ Stimulate Fibrosis deposition

CKD stages


Albuminuria categories
(mg/g creatinine)
A1
A2
A3
< 30
30–300
> 300
GFR categories
(ml/min x 1.73 m²)
G1
≥ 90
G2
60–89
G3a
45–59
G3b
30–44
G4
15–29
G5
< 15
G5 D/T
Kidney failure
Usually defined by KRT

ORIGINAL RESEARCH

UNDER-DIAGNOSED CHRONIC KIDNEY DISEASE IN JORDANIAN ADULTS: PREVALENCE AND CORRELATES

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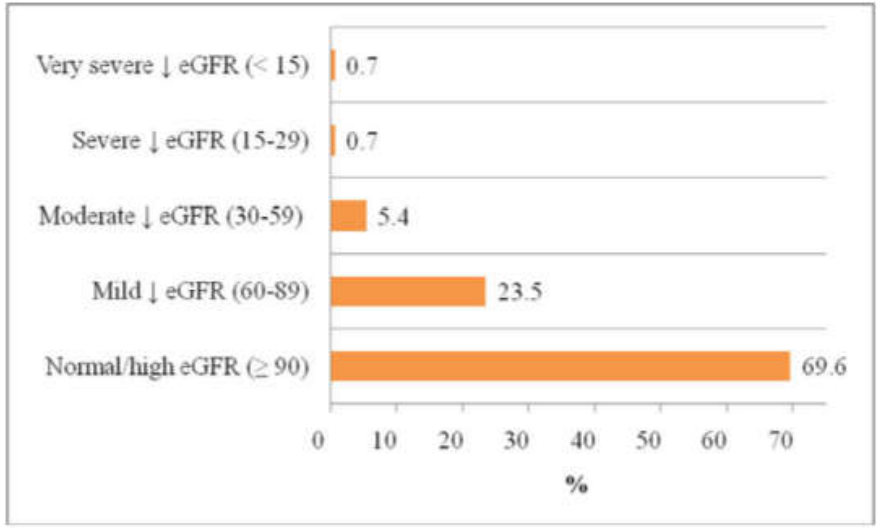
Epidemiology

- 10% of the adult population around the world have CKD stages 1–5
- Registration and diagnosis (variable between countries)
- found that approximately 31% of the individuals (at high risk) had unrecognised CKD eGFR < 90.
- 7% of the present sample had an eGFR of
- Mortality is higher than non CKD



Risk factors

- Individuals with any of the following attributes are at high risk for CKD and could benefit from screening:

1- age more than 60 years

2- Diabetes mellitus (DM)

3- Hypertension (HTN)

4- Family history of kidney diseases

Leading causes of CKD

1- Diabetes
2- Hypertension
3- Obstructive nephropathy (kidney stones, BPH)
4- Kidney diseases (TIN, GN, ADPKD, recurrent UTI and pyelonephritis)
5- Renovascular diseases → Renal artery stenosis
Fibromuscular dysplasia (FMD)
6- Some medications - for example, NSAIDs, Heavy metals
7- Fetal developmental problem → Reflux → كلية ناقصة

Vesicoureteral reflux (VUR) is a condition in which urine flows backward from the bladder to one or both ureters and sometimes to the kidneys. VUR is most common in infants and young children. Most children don't have long-term problems from VUR.

8- Infections like Hep C and HIV, Malaria and yellow fever
9- Illegal substance abuse - such as heroin or cocaine.
Injury - a sharp blow or physical injury to the kidney

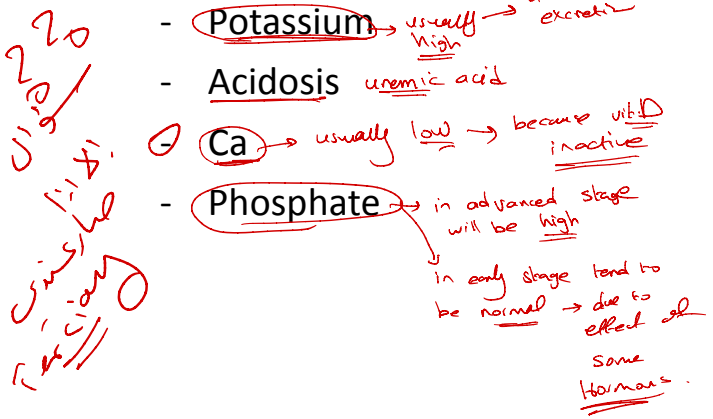
Clinical manifestation

- **Urinary:**
- Urine output: polyuria, oliguria, anuria
- Frothy, hematuria

- **Uremia:** accumulation of waste product (protein metabolism)

- **Volume:** hypervolemia

- **Acid base, electrolytes:**
- Sodium
- Potassium
- Acidosis
- Ca
- Phosphate



- **Hematological**
- Anemia
- Bleeding: platelets dysfunction (due to uremia)

- **Infection:**

- **CVS**: CAD, HF, LVH, arrhythmia, pericarditis
- **RS:** pulmonary edema
- **GI:** N/V, ulcer, uremic fetor
- **Neuro:** encephalopathy, peripheral neuropathy, restless leg syndrome

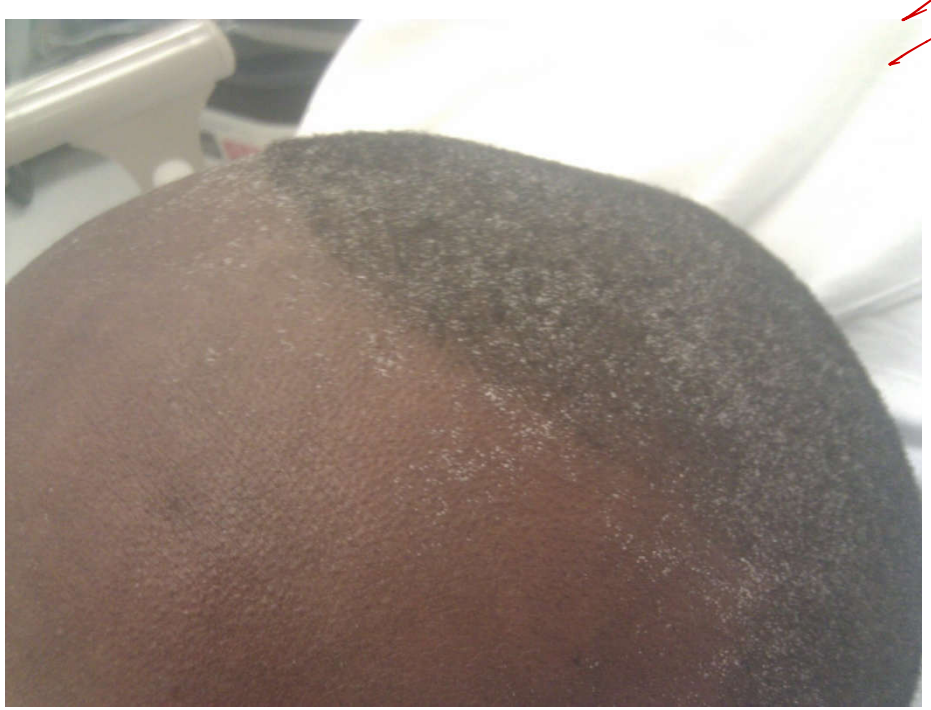
2 (*) Urea by it self is not toxin to the tissue
But its marker

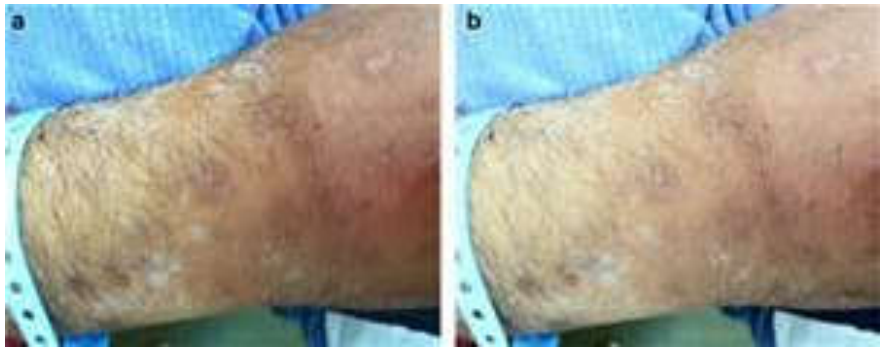
- **Skin**
- Earthy color → accumulation of Nitrogenous waste product.
- Pruritus
- Petechiae, ecchymosis
- Nail changes

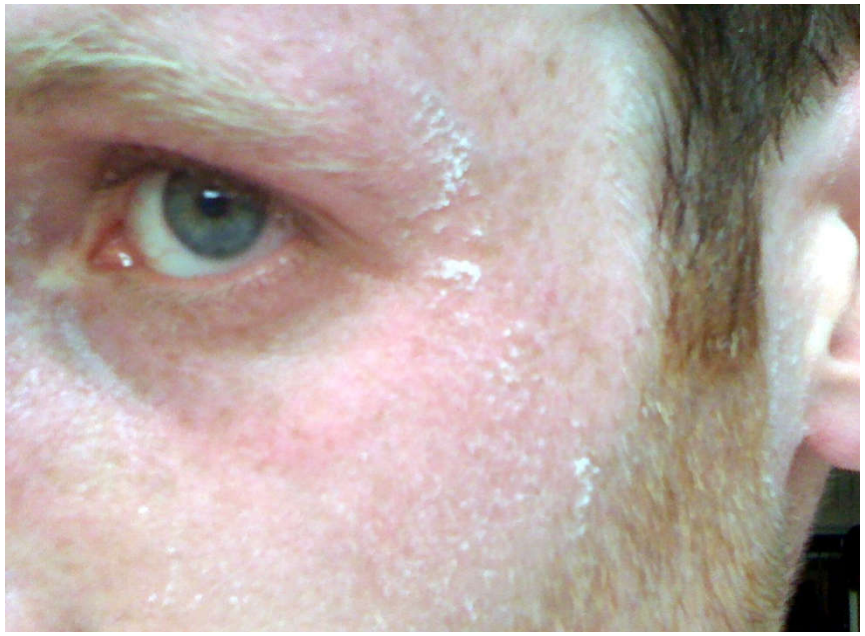
Uremic Forest

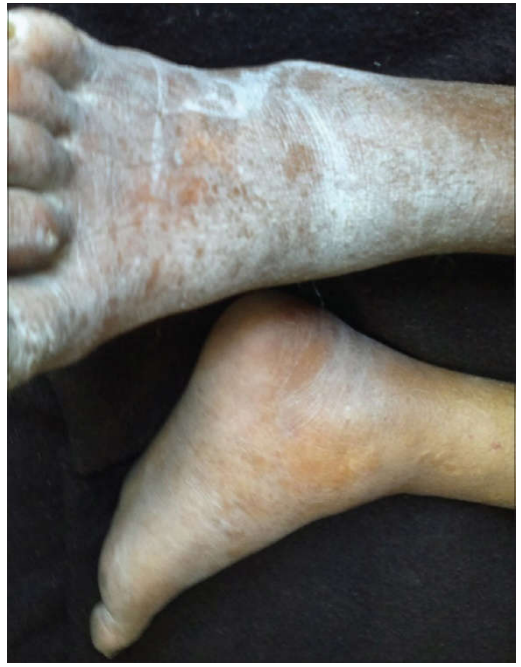
whitish color on the skin ← الصقيع

Frost الصقيع





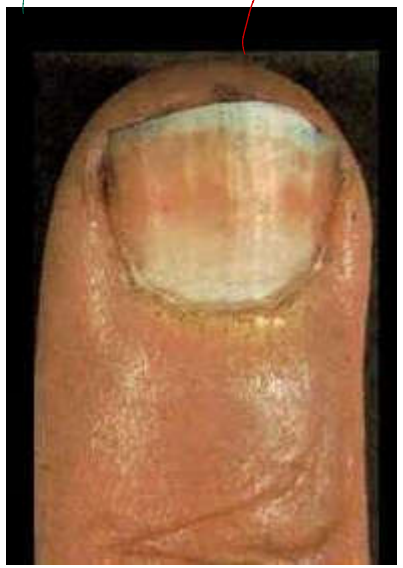


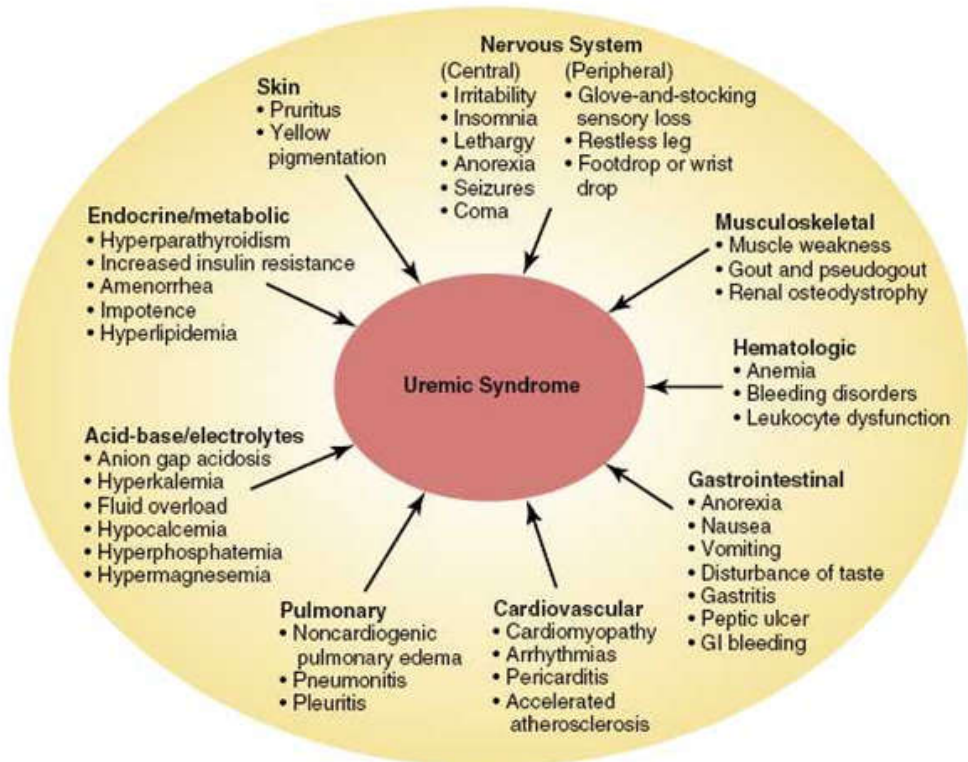


Earthy color

→ lindsay's nail → white/brown "half-and-half" nail occur in CKD

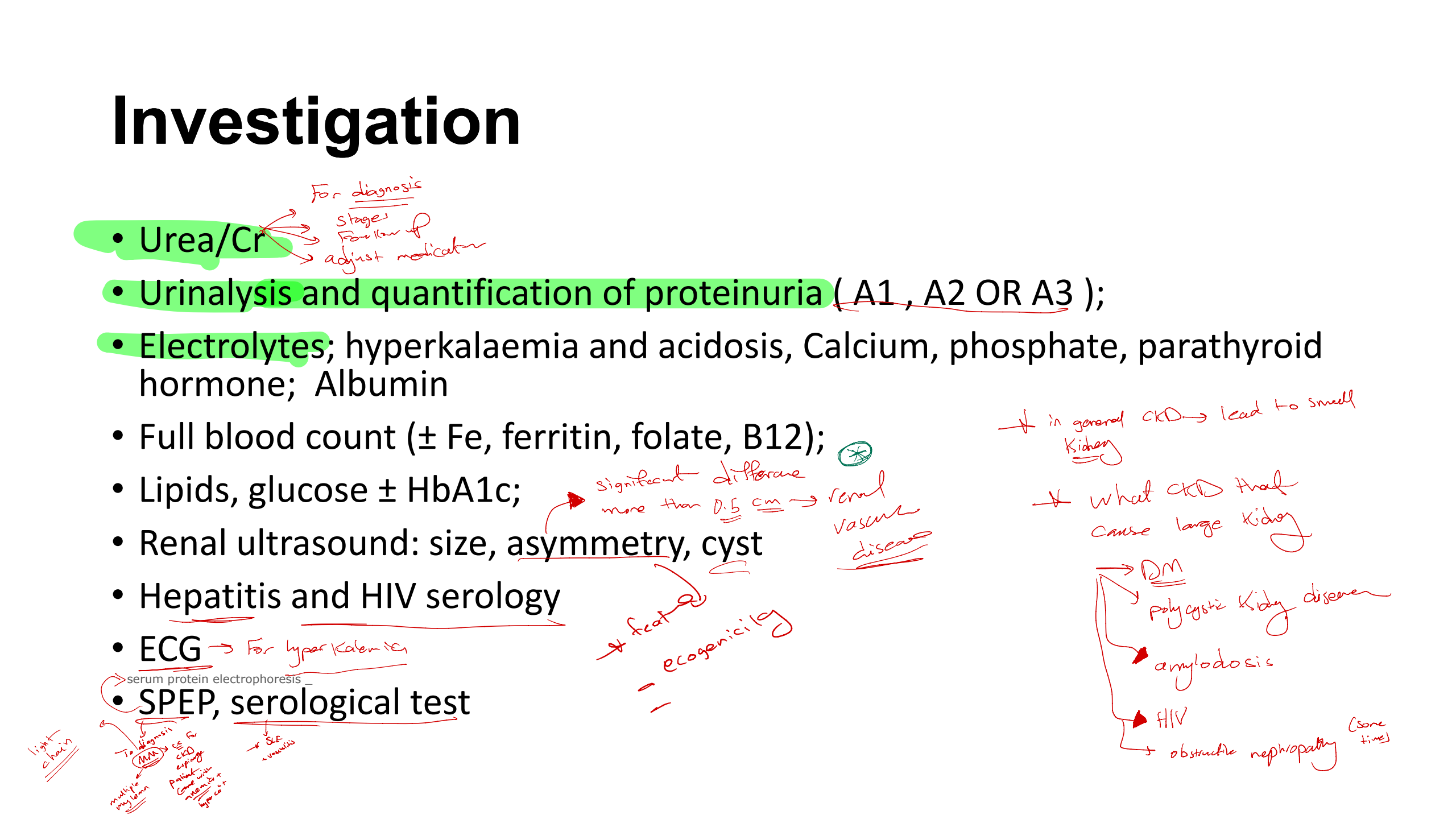
half and half nail due to uremic toxin and hypoalbuminae




Nervous System
(Central)
• Irritability
• Insomnia
• Lethargy
• Anorexia
• Seizures
• Coma
(Peripheral)
• Glove-and-stocking sensory loss
• Restless leg
• Footdrop or wrist drop
Skin
• Pruritus
• Yellow pigmentation
Endocrine/metabolic
• Hyperparathyroidism
• Increased insulin resistance
• Amenorrhea
• Impotence
• Hyperlipidemia
Musculoskeletal
• Muscle weakness
• Gout and pseudogout
• Renal osteodystrophy
Hematologic
• Anemia
• Bleeding disorders
• Leukocyte dysfunction
Uremic Syndrome
Acid-base/electrolytes
• Anion gap acidosis
• Hyperkalemia
• Fluid overload
• Hypocalcemia
• Hyperphosphatemia
• Hypermagnesemia
Gastrointestinal
• Anorexia
• Nausea
• Vomiting
• Disturbance of taste
• Gastritis
• Peptic ulcer
• GI bleeding
Pulmonary
• Noncardiogenic pulmonary edema
• Pneumonitis
• Pleuritis
Cardiovascular
• Cardiomyopathy
• Arrhythmias
• Pericarditis
• Accelerated atherosclerosis

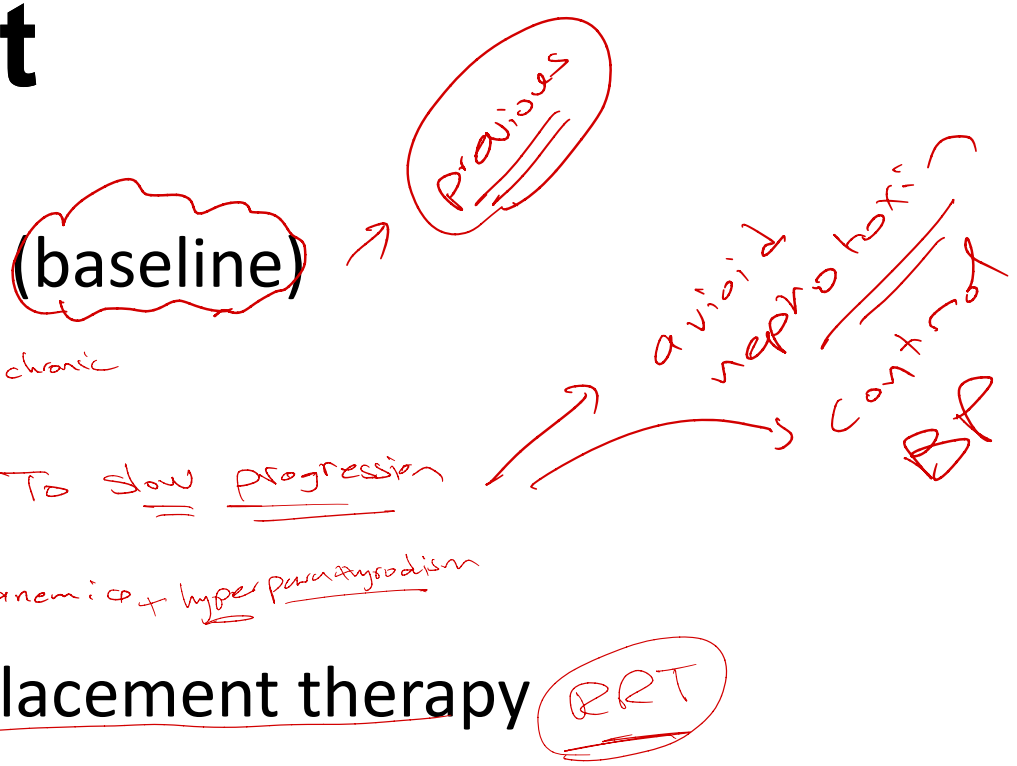
Investigation

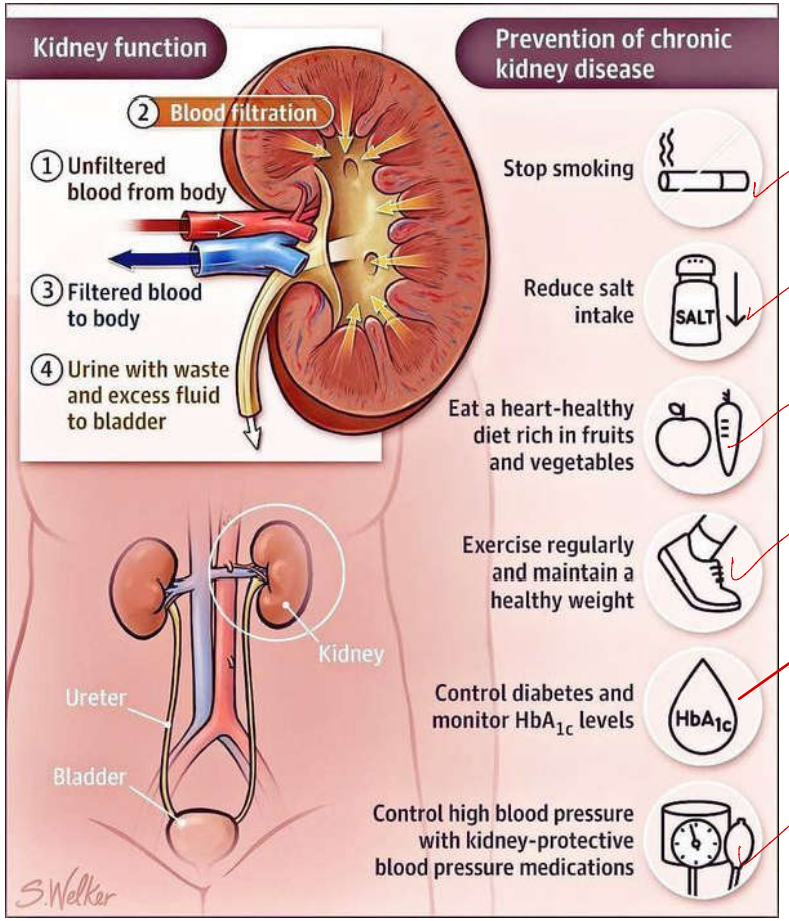
- Urea/Cr
- Urinalysis and quantification of proteinuria (A1 , A2 OR A3);
- Electrolytes; hyperkalaemia and acidosis, Calcium, phosphate, parathyroid hormone; Albumin
- Full blood count (± Fe, ferritin, folate, B12);
- Lipids, glucose ± HbA1c;
- Renal ultrasound: size, asymmetry, cyst
- Hepatitis and HIV serology
- ECG
- SPEP, serological test



Management

- Acute versus chronic (baseline)
- Reversibility
- Retard progression
- Treat complication
- Prepare for renal replacement therapy




Kidney function
2 Blood filtration
1 Unfiltered blood from body
3 Filtered blood to body
4 Urine with waste and excess fluid to bladder
Kidney
Ureter
Bladder
S.Welker
Prevention of chronic kidney disease
Stop smoking
Reduce salt intake
SALT
Eat a heart-healthy diet rich in fruits and vegetables
Exercise regularly and maintain a healthy weight
Control diabetes and monitor HbA1c levels
HbA1c
Control high blood pressure with kidney-protective blood pressure medications

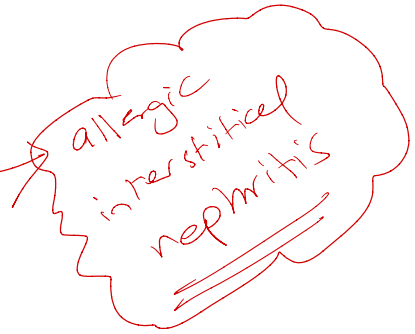
AKI or CKD

	Acute Kidney Injury	Chronic Kidney Disease
History	Short duration History of acute illness	Long duration History of kidney disease and/or causative co-morbidity
Examination	Acutely ill May have hypotension, fluid overload, metabolic acidosis,	Better toleration of biochemical abnormalities Anaemia, cachexia, grey discolouration of skin
Creatinine	Rapidly increasing values	History indicating derangement Stable serial measurements
Calcium	Usually normal	Low in untreated chronic disease
Haemoglobin	May be normal or low	Due to erythropoietin deficiency- chronic normocytic anaemia
Renal ultrasound	Often normal When the cause is acute obstruction- hydronephrosis	Scars from reflux nephropathy Renovascular disease- asymmetry Large kidneys in • Diabetes, • Amyloidosis, • Chronic Hydronephrosis • Polycystic Kidney disease

Adapted from Hall (2008)

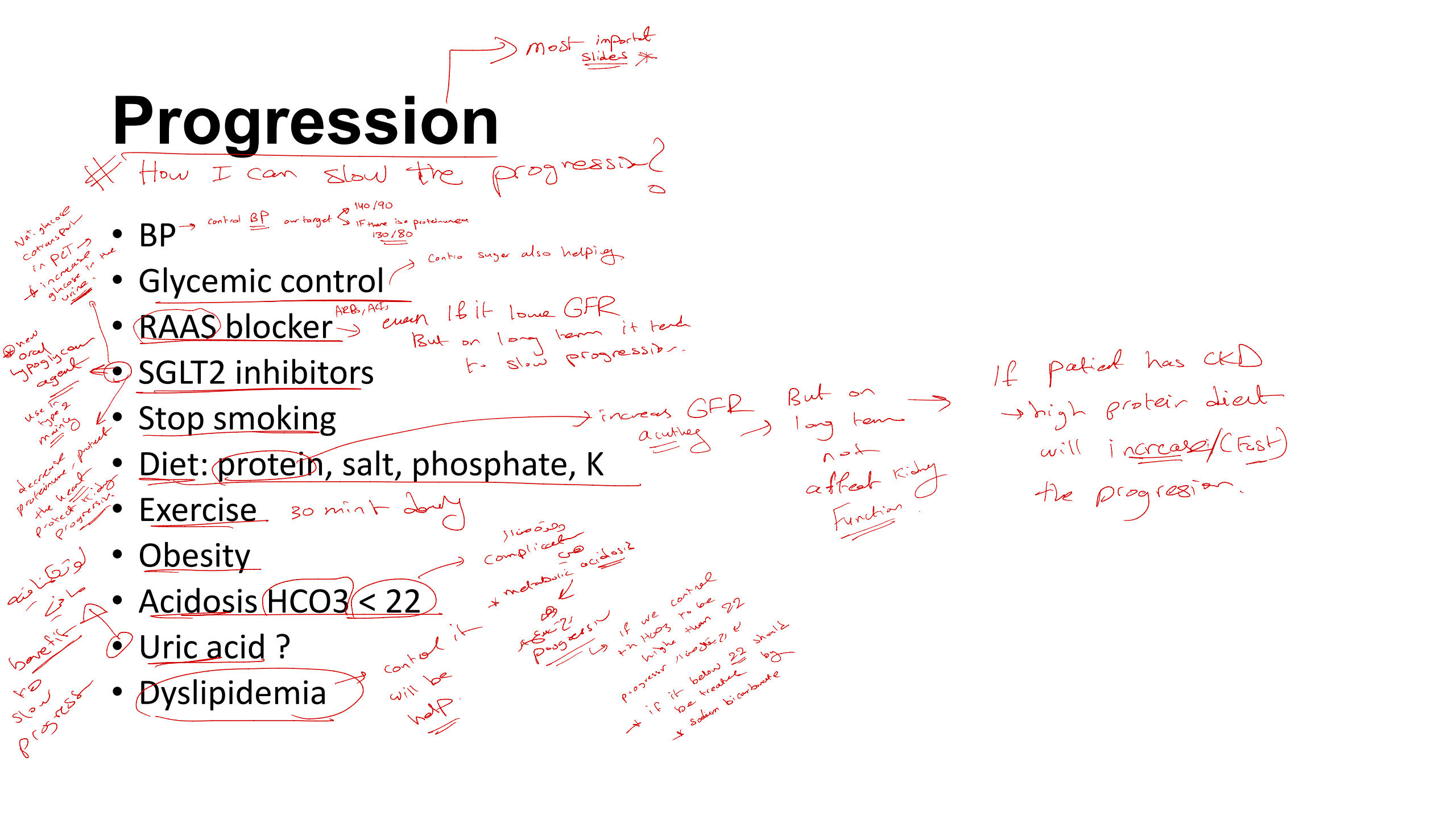
Treat the cause

- GN
- Pyelonephritis
- AIN
- Obstruction
- Renovascular disease



Progression

- BP
- Glycemic control
- RAAS blocker
- SGLT2 inhibitors
- Stop smoking
- Diet: protein, salt, phosphate, K
- Exercise
- Obesity
- Acidosis HCO3 < 22
- Uric acid ?
- Dyslipidemia



should be adjusted according to GFR.

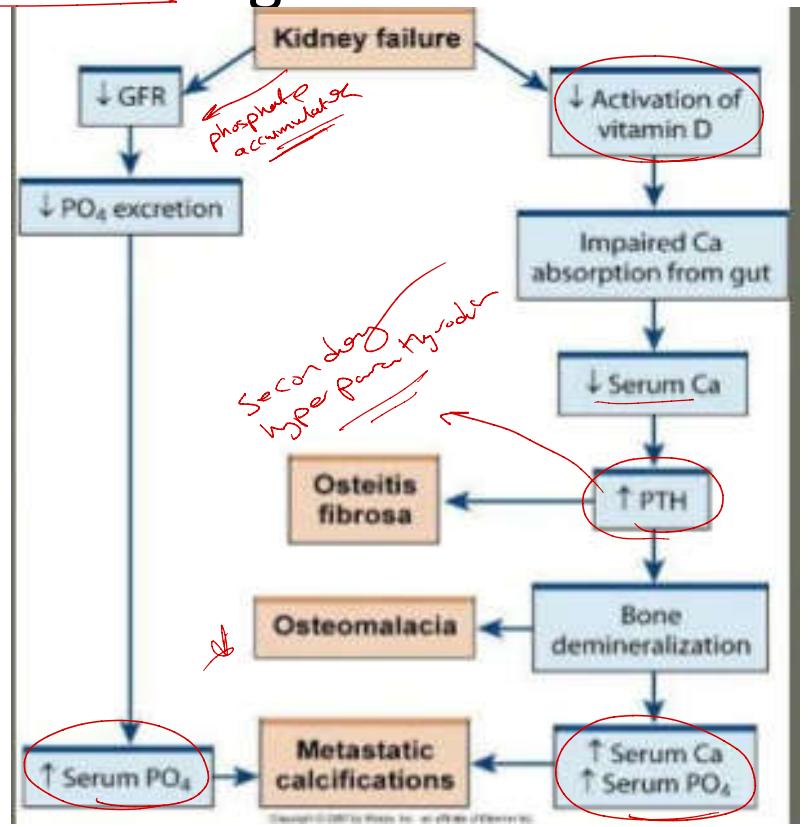
Table 33-4 Drug Dosages in Chronic Kidney Disease

Major Dosage Reduction	Minor or No Reduction	Avoid Usage
Antibiotics		
Aminoglycosides	Erythromycin	
Penicillin	Nafcillin	Nitrofurantoin
Cephalosporins	Clindamycin	Nalidixic acid
Sulfonamides	Chloramphenicol	Tetracycline
Vancomycin	Isoniazid, rifampin	
Quinolones	Amphotericin B	
Fluconazole	Aztreonam, tazobactam	
Acyclovir, ganciclovir	Doxycycline	
Foscarnet		
Imipenem		
Others		
Digoxin	Antihypertensives	Aspirin
Procainamide	Benzodiazepines	Sulfonylureas
H_2 antagonists	Quinidine	Lithium carbonate
Meperidine	Lidocaine	Acetazolamide
Codeine	Spironolactone	NSAIDs
Propoxyphene	Triamterene	Phosphate-containing bowel-preps

1. Cockcroft-Gault Equation (mL/min)	$CCr = \frac{(140 - age) \times LBW\ [kg]}{Cr\ [mg/dL] \times 72}$ *For women Multiply by 0.85*
2. MDRD study equation (mL/min/1.73 m²)	$GFR = 186.3 \times (SCr)^{-1.154} \times (Age)^{-0.203}$ *Multiply by 0.742 for women* *Multiply by 1.21 for African ancestry*
3. CKD-EPI equation	$GFR = 141 \times \min(SCr/\kappa)^{\alpha} \times \max(SCr/\kappa)^{-1.209} \times 0.993^{age}$ *Multiply by 1.018 for women* *Multiply by 1.159 for African ancestry* **κ** is 0.7 for females and 0.9 for males, **α** is –0.329 for females and –0.411 for males, **min** indicates the minimum of SCr/κ or 1, & **max** indicates the maximum of SCr/κ or 1

Complication

- Treat anemia target (Hb: 10-11)
- Secondary hyperparathyroidism (by vitamin D & Calcium to correct phosphate actually (calcium-based phosphate binder) or (Sevelamer / renagel (non calcium-based phosphate binder) in case of high calcium)
- CV disease (aspirin and statins)



RRT

- Transplant
- Hemodialysis
- Peritoneal dialysis
- Artificial kidney
- Animal kidney ?