Hereditary Diseases of the Kidneys

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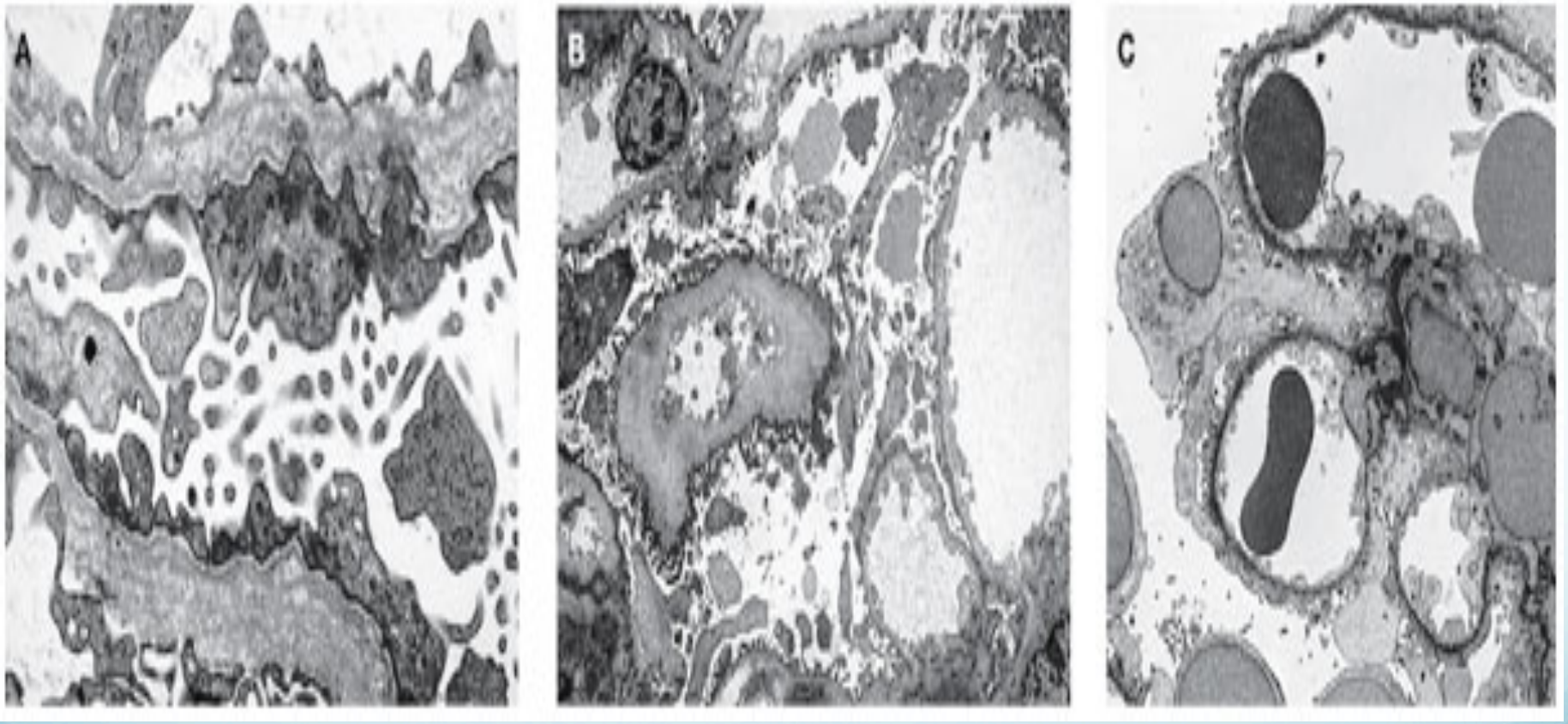
Hereditary Disease of the kidneys - Summary

- Glomerular diseases
- Hereditary Cystic Diseases
- Hereditary Nephroses
- Wilms Tumor
- Reflux Nephropathy
- Hereditary Stone Diseases

Hereditary Glomerular Diseases

- Alports Syndrome
  - Hereditary Nephritis with sensorineural deafness, corneal opacities (in some Kindreds)
    - Genetic disorder of the Alpha subunit of Type 4 collagen.
  - Benign Familial Hematuria
    - Also known as Thin Basement membrane Disease
  - Nail Patella Syndrome
    - Hereditary Nephritis with finger nail disorder, patellar problems and ischial horn formation.
    - Different collagen gene is affected.

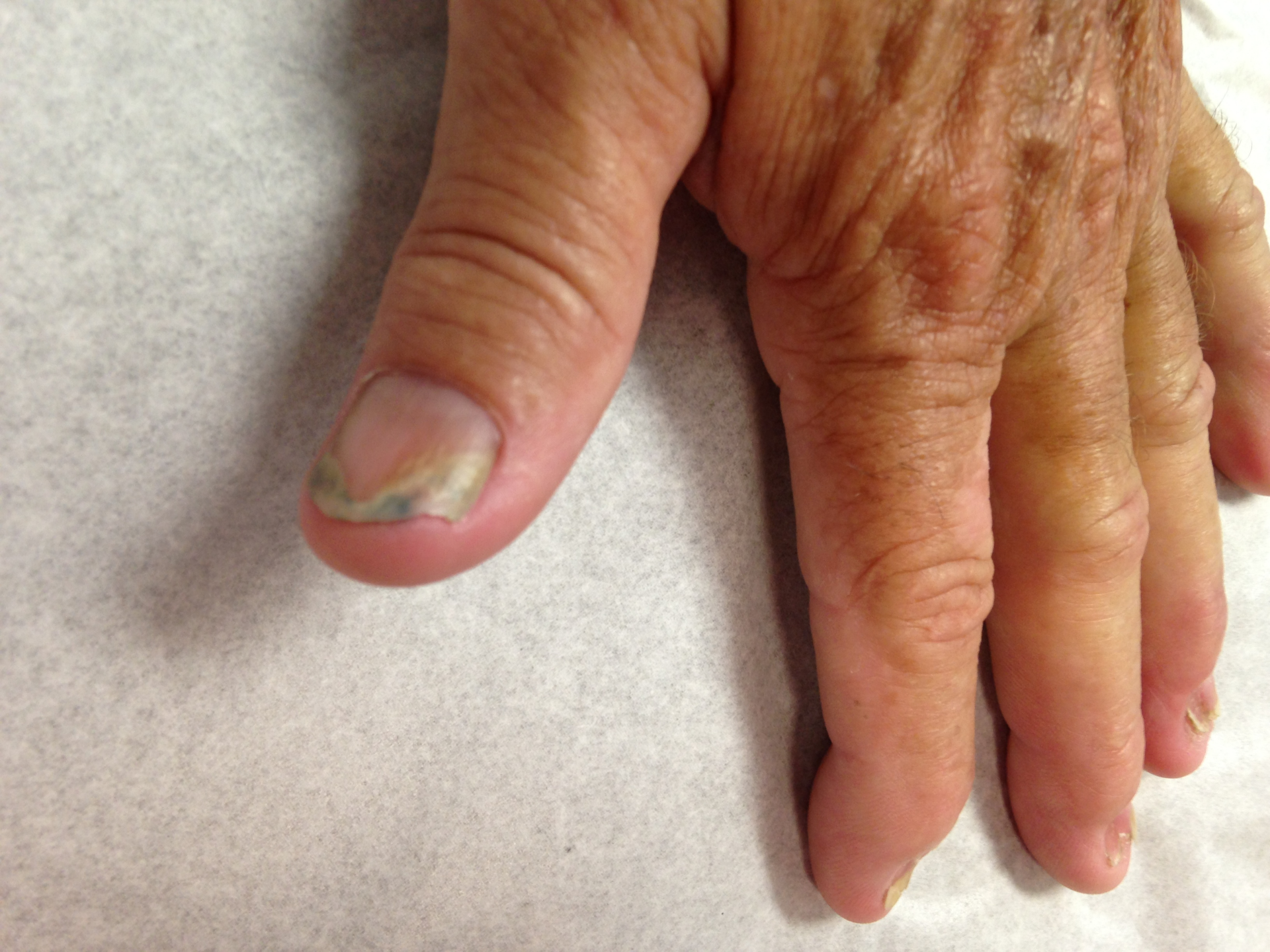
Hereditary Nephritis



Alports Nail -Patella Thin Basement Mem.

Nail Patella Syndrome

Note how the nail findings lessen further from Thumb



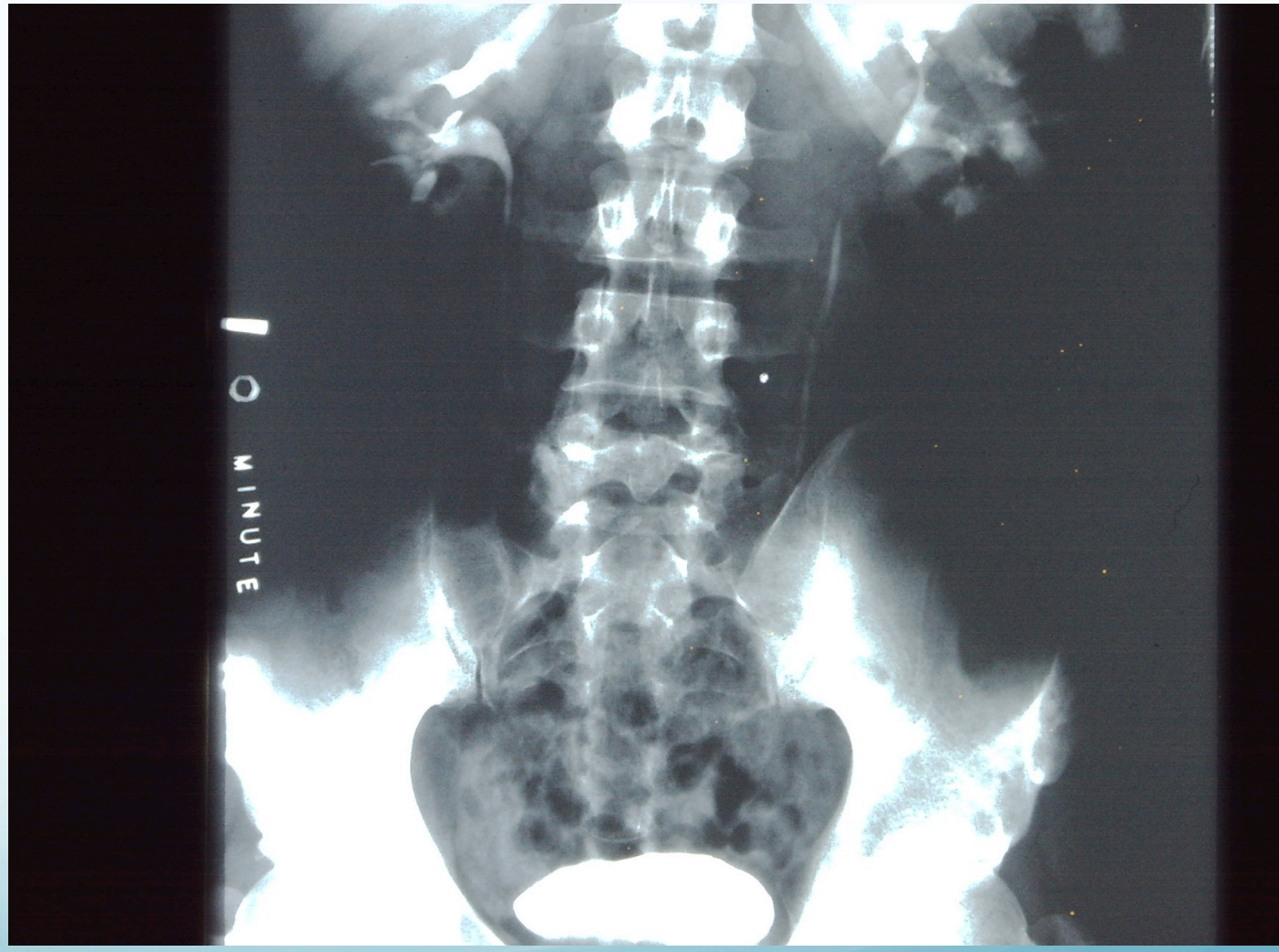
Hereditary Cystic Diseases

- Polycystic Kidney Disease PCKD or PKD
  - Autosomal dominant – most common type
    - Cysts in Kidneys, Liver, spleen, ovaries
      - Carolies disease (cystic dilation of pancreatic duct) makes risk for recurrent pancreatitis
    - Mitral regurgitation
    - Berry Aneurysms
    - Hepatic fibrosis with hypersplenism and thrombocytopenia
  - Autosomal recessive PKD shows up in children - much earlier presentation, as both genes are affected.
    - Variceal hemorrhage is common initial presentation, due to hepatic fibrosis and cirrhosis.

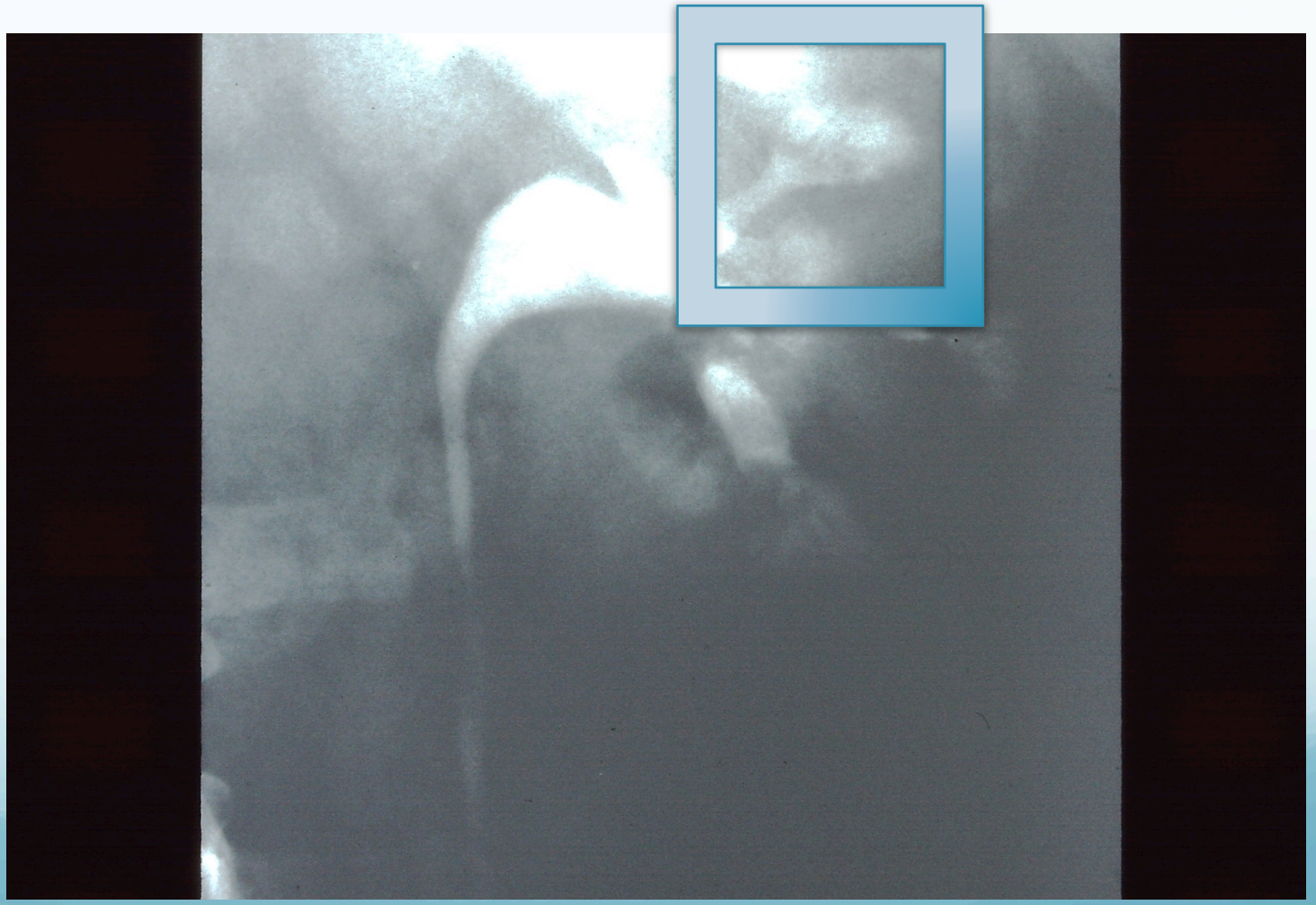
Hereditary Cystic Diseases

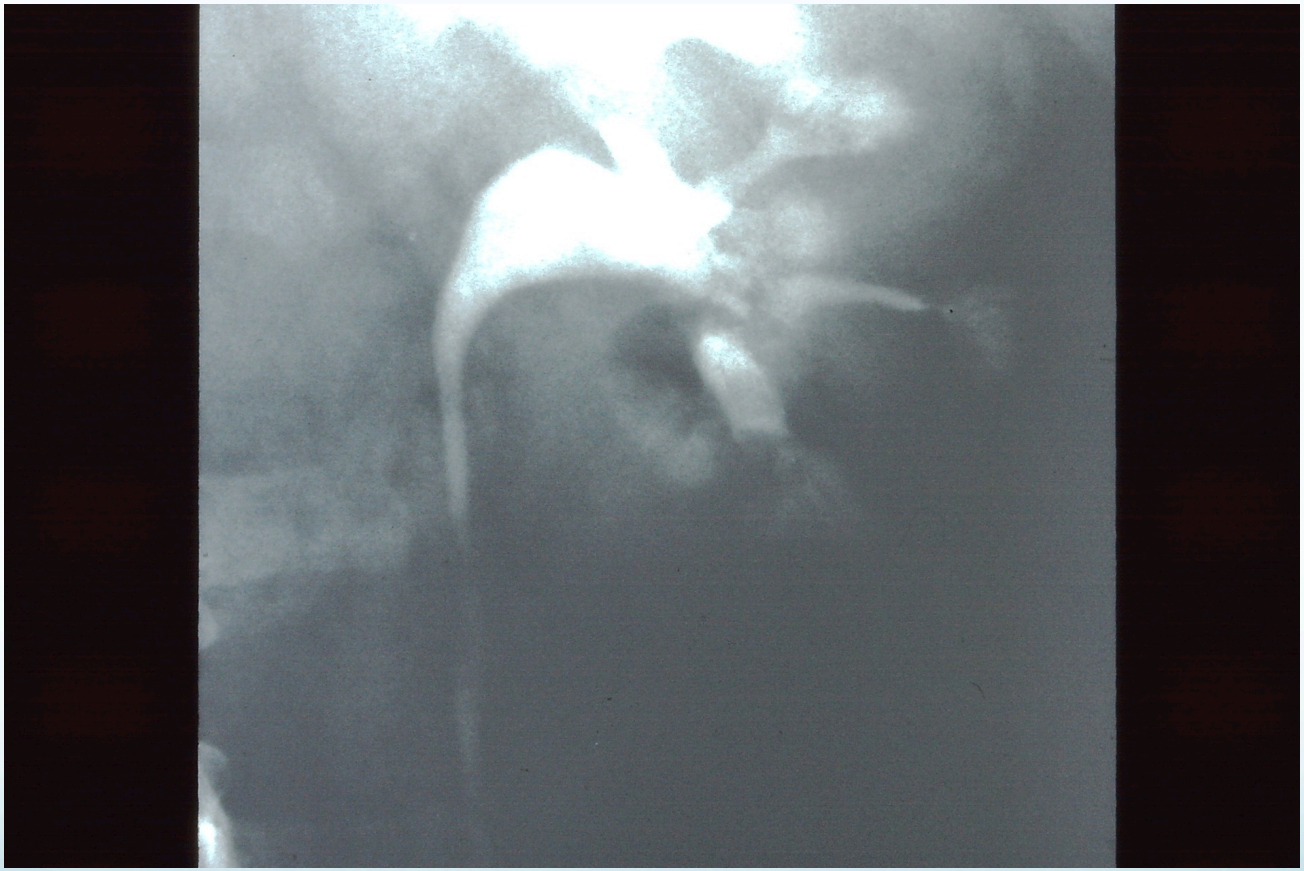
- Polycystic Kidney Disease PCKD or PKD
  - See separate lecture and case study
- Medullary Sponge Kidney
  - Dilation of collecting ducts
    - Leads to slower flow of urine and precipitation of calcium – bouquet of Flowers sign on Xray
    - Kidney stones

IVP
chronic hematuria



Bouquet of flowers on IVP





Hereditary Cystic Diseases

- Hereditary Nephroses
  - Hereditary condition that presents early in life with multicystic kidneys and nephrotic syndrome.
  - Seen in Pediatric nephrology.

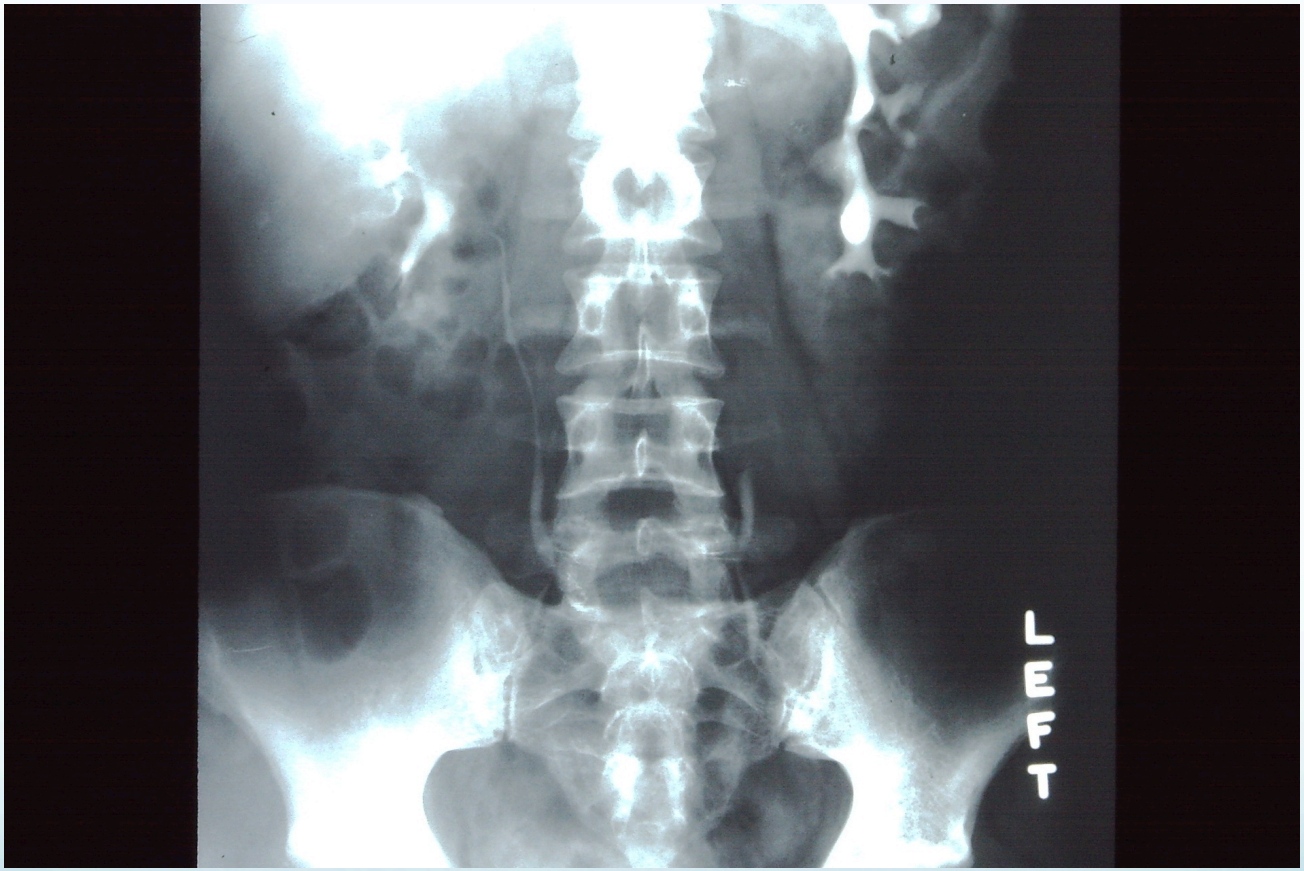
Reflux Nephropathy

- Embryology of the kidneys:
  - Start with 6 segments along spine – 3 on each side
    - The 3 proto-kidneys fuse to form one kidney on each side
    - All 6 or parts of the kidneys can fuse and form a "horseshoe kidney" or malrotate
    - One of the segments may not fuse normally and result in duplicated artery/ vein or Ureter on one side
    - The ureter forms from the kidney down, AND from the bladder up.
    - The transition point for blood flow from the bladder vs the kidney is variable
    - The ureter may not connect properly to the bladder

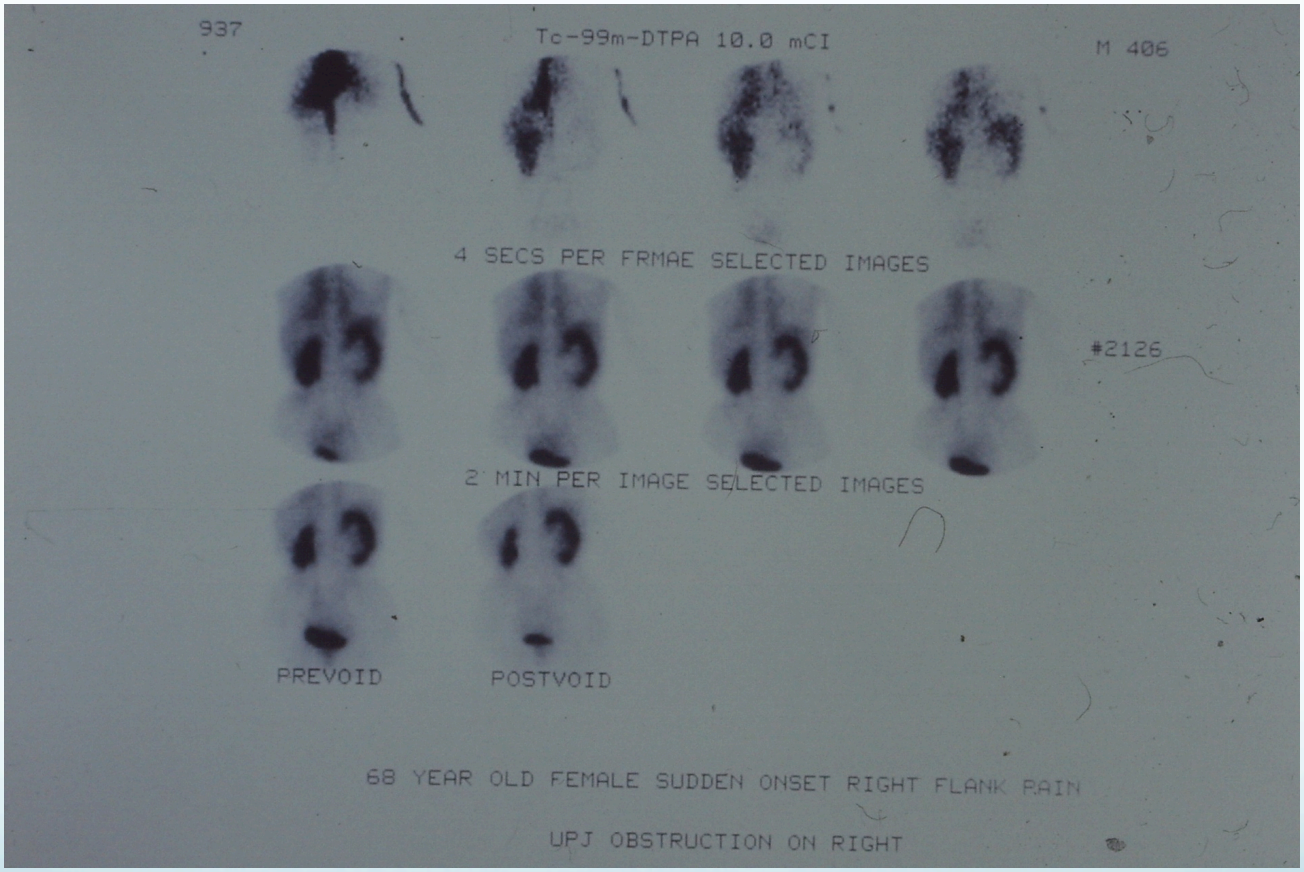
Reflux Nephropathy

- Embryology of the kidneys:
  - The ureter may not connect properly to the bladder
  - Normally there is a valve that keeps urine from refluxing back to the kidney when the bladder contracts
  - When the valve malfunctions, urine is pushed back up the ureter under pressure, and can cause scarring in the kidney on that side
  - This is called Reflux Nephropathy.

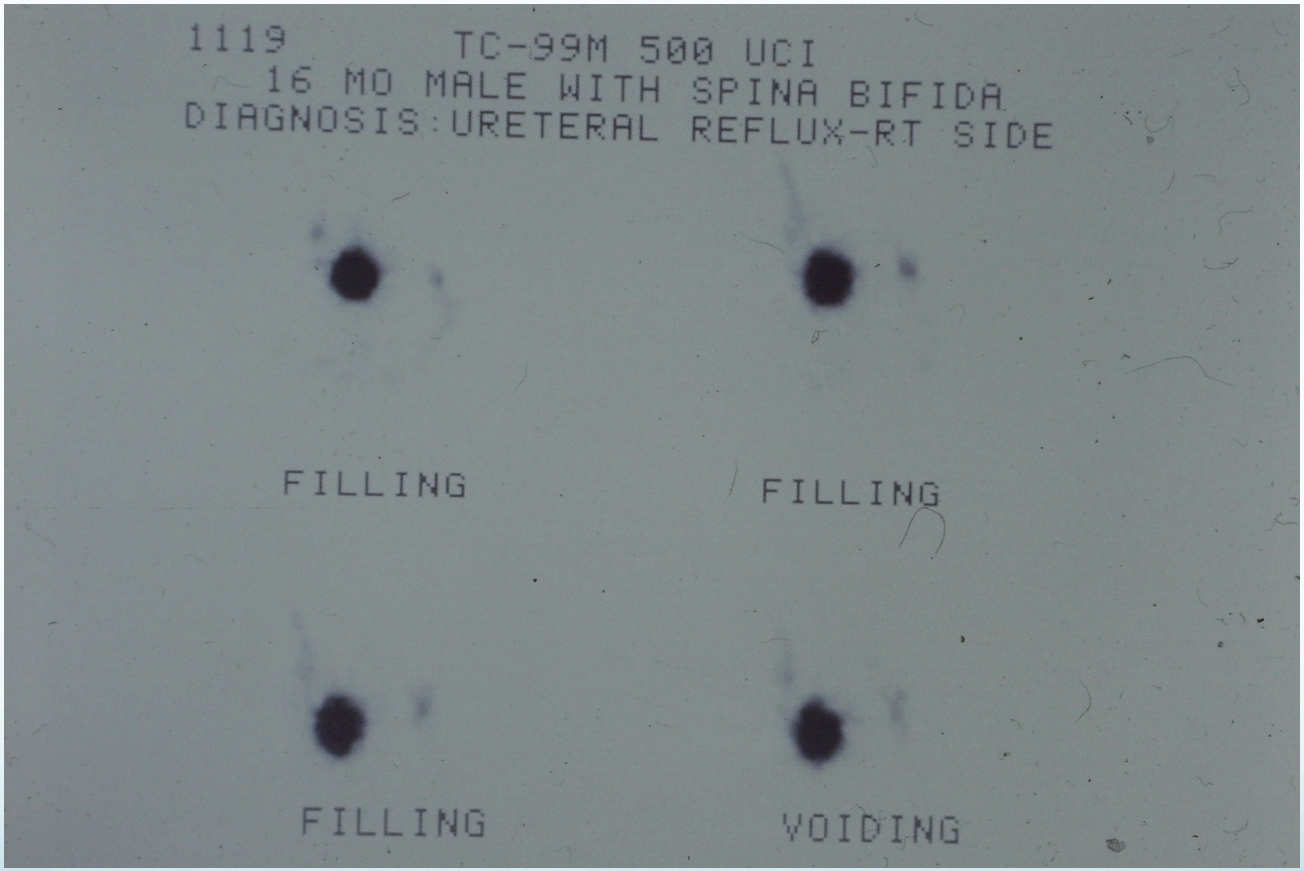
IVP with duplicated collecting system on left – hint that reflux may have been present



Female with recurrent kidney stones on Right



16 year old with right sided Ureteral Reflux



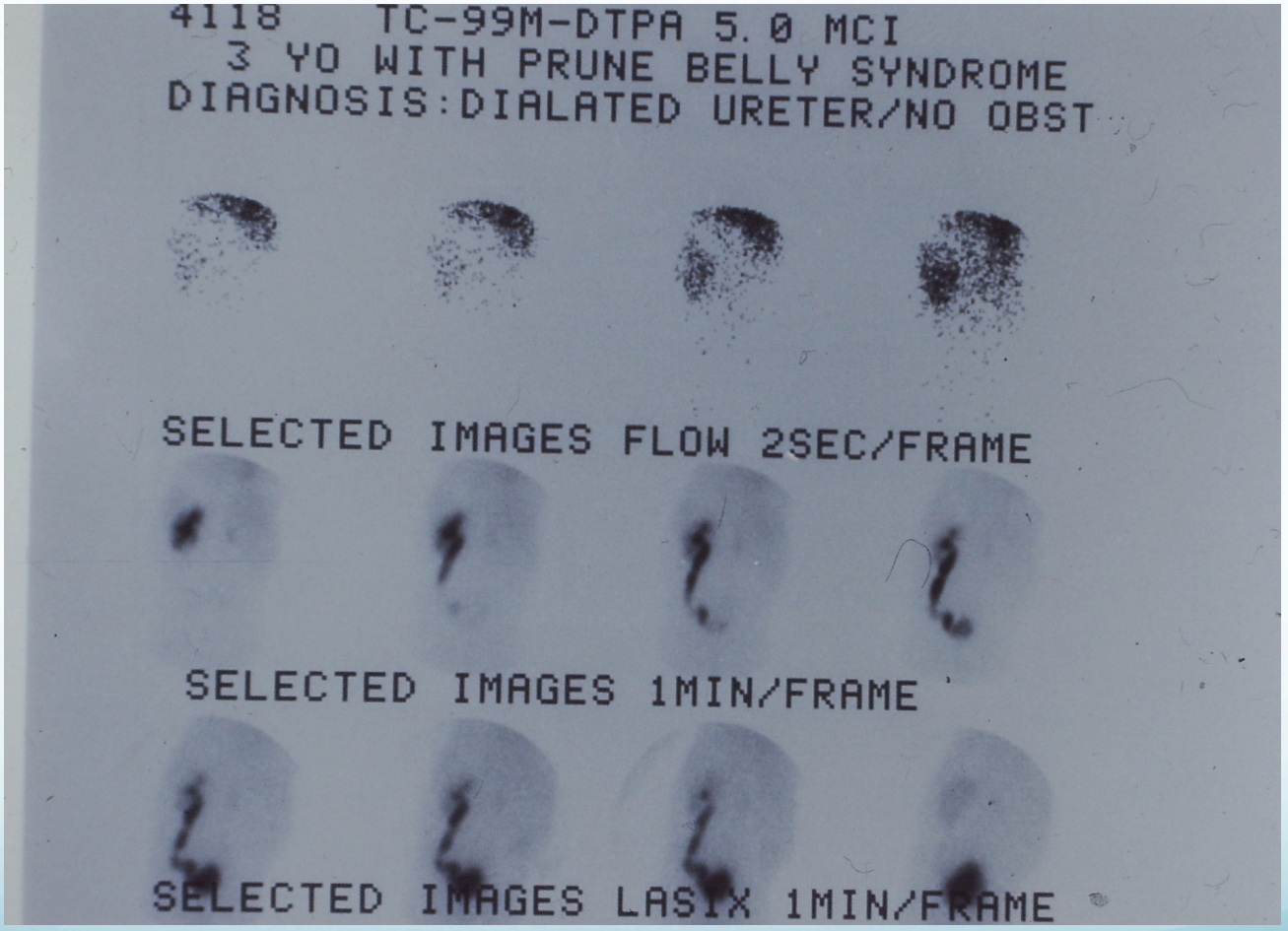
Reflux Nephropathy

- Presentations:
  - Recurrent UTI's in childhood or during pregnancy
  - Hypertension presenting in Teens/ 20's
    - Reflux is most common etiology for hypertension in Teen girls
  - Recurrent kidney stones on one side
  - Biopsy of kidney shows focal segmental glomerulosclerosis
  - Proteinuria with Hypertension
  - Glomerular scarring / thinning in upper or lower poles on US.

Reflux Nephropathy

- Presentations:
  - Prune Belly Syndrome
    - Reflux
    - Loss of abdominal wall musculature
    - Renal failure

Nuclear Renal scan with lasix washout



Congenital tumor of Kidney

- Wilm's Tumor

Hereditary kidney stone disorders

- Medullary Sponge kidney
- Reflux Nephropathy
- RTA's
- Hypercalciuria Syndromes

RTA's

- Named according to order in which they were described, i.e. severity.
- Type I is worst showing up in children with failure to thrive, Ricketts, hypokalemia, stones
- Type II also shows up in children, but not as severe.
- Type III rare
- Type IV not described until diabetics lived long enough to develop renal comps.

Renal Tubular Acidosis

- Type I most severe, occurs in the Distal tubule, and is congenital problem with the transport proteins responsible for excretion of acid.
- Four types of Type I distal RTA:
  - Rate dependent (defective or decreased pump)
  - Secretory (absent proton pump),
  - Gradient dependent (Backleak of K)
  - Voltage dependent (defective K channels)
    - Seen in sickle cell, obstructive uropathy
    - Potassium channels affected by Amiloride, lithium
- Bicarb can go as low as 8
- HypOkalemia (hypERkalemia in voltage dependent)

Renal Tubular Acidosis

- Type II Proximal Tubular Acidosis
  - Less severe, immaturity of proximal tubule leads to bicarb loss.
  - Corrects during puberty
  - Bicarb usually 15 or greater
  - HypOkalemia
  - Large bicarb requirement
  - Stones, Failure to thrive.
  - 11 types associated with conditions such as myeloma, Fanconi's syndrome.

Type II Proximal RTA subtypes

- Hereditary
  - Fanconi syndrome
  - Wilson's dz, Cystinosis
  - Tyrosinemia, Pyruvate Carboxylase Deficiency
- Acquired
  - 1. Drugs (TCN, Gent, **Glue sniffer**, GMP)
  - 2. Heavy Metals
  - 3. Immunologic disease (sjogrens, **Myeloma**)
  - 4. Balkan nephropathy
  - 5. Nephrotic syndrome/ transplant dysfunction
  - 6. Osteoporosis
  - 7. PNH

Acquired Fanconi's Syndrome

- Features:
  - Glucosuria with normal serum glucose
  - Metabolic acidosis with bicarbonate wasting in urine
  - Phophaturia
  - Hypokalemia, hypouricemia, hypophosphatemia
- Most commonly due to drug toxicity

Thomas DeCato, Tenofovir induced Fanconi Synd. ACP Hospitalist Nov 2014. Pg 33

Acquired Fanconi's Syndrome

- Most commonly due to drug toxicity
  - Can appear after years of exposure
  - Can take weeks to months to resolve
  - Recovery may be incomplete
- Drugs that cause Fanconi syndrome:
  - Platinum and alkalating chemotherapy agents
  - Aminoglycosides
  - Valproic acid
  - Tenofovir and many other antiviral agents.

Renal Tubular Acidosis

- Type III
  - Small kindred of children born with Combo of type I distal RTA AND tubular immaturity of proximal tubule type II RTA. Have features of both, and the proximal tubule disorder corrects after puberty, leaving them with a true Type I distal RTA.

Renal Tubular Acidosis

- Type IV RTA
  - Also known as Hypoaldosteronism, Hyporeninism.
  - Problem with ammoniagenesis
  - Commonly seen in Diabetics, Sarcoidosis, Chronic Pyelonephritis, Gouty nephropathy, chronic rejection
  - Bicarb as low as 18, may be 22
  - HypERkalemia out of proportion to their renal dysfunction.

Type IV RTA subtypes

- Aldosterone Deficient
  - 1. Adrenal Insufficiency
  - 2. Hyporenin/hypoaldo (seen in Diabetics)
  - 3. Chloride shunt (Gordon's syndrome)
- Aldosterone Resistant
  - 4. PseudohypoAldosteronism
    - Will have HIGH levels of aldo: receptor is damaged
    - Pseudo-pseudo-hypoaldo patients have phenotype, but normal aldosterone function
  - 5. Early childhood type IV RTA from interstitial disease

Diagnosis

- First you must suspect RTA in patients with
  - Unexplained bone disease
  - Muscle weakness
  - Nephrocalcinosis
  - Glycosuria/aminoaciduria
  - Kidney stones
  - Non-Gap metabolic acidosis
  - Failure to thrive in children
  - Associated diseases (Diabetes, Gout, Myeloma)

Diagnosis of RTA

- Workup
  - Lytes and BUN/Creat
    - Measured bicarb < 15 is Type I RTA
    - Bicarb 15-18 is Type II proximal RTA
    - Bicarb > 18 with high K is Type IV RTA
  - Urine pH in basal state AND during bicarb supplementation
    - Urine pH > 7 means pt is spilling bicarbonate into urine (i.e Type II proximal RTA)
    - Urine pH > 6 in pt with severe acidosis probably means they are unable to excrete an acid load (Type I Distal RTA)
  - Urine pCO2 (normal level = 32.7 +/- 3 mm/Hg)

Hypercalciuria Incidence

- Stones account for 7-10 per 1000 hospital admissions
- 12% of population will form a stone during their lifetime
- Men affected 2-3x more than women
- Peak onset third decade
- Highest incidence in fifth and sixth decades

Stone Composition

- Calcium oxalate alone or with apatite= 60-70%
- Pure apatite= 7%
- Brushite (calcium monohydrogen phosphate dihydrate)= 1%
- Struvite (magnesium ammonium phosphate hexahydrate)= 10-20%
- Uric acid=5-10%
- Cystine= 1-2%

Stone Composition- Rare Stones

- Xanthine stone- xanthine oxidase deficiency
- 2,8-dihydroxyadenine stones- adenine phosphoribosyltransferase deficiency
- Acid ammonium urate stones- chronic diarrhea and hypokalemia
- Oxypurinol and xanthine stones- pts taking allopurinol

Stone Composition- Rare Stones

- Triamterene stones- pts taking triamterene
- Protein “matrix” stones

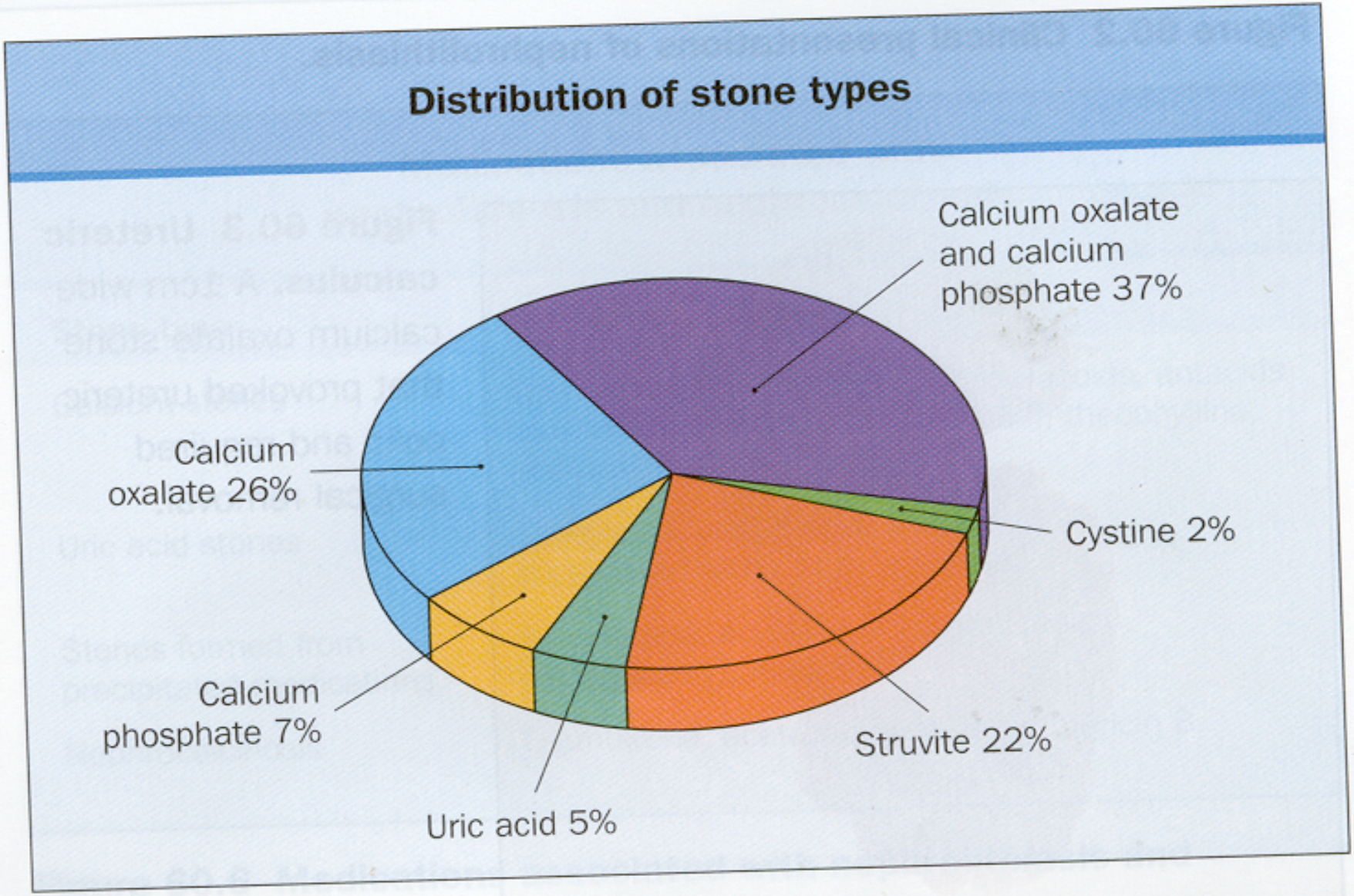


Figure 60.1 Proportion of stone types in a typical US population.

Cystine Stones

- Cystinuria is a rare hereditary disorder
  - tubular defect in dibasic amino acid transport
  - Increased cystine, ornithine, lysine and arginine excretion
- Stones seen by fourth decade
- Staghorn or multiple bilateral stones

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