The Annual General Pediatric Review & Self Assessment

Nicklaus Children's Hospital

# NEPHROLOGY


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# To be discussed

- Proteinuria/Nephrotic Syndrome
- Hematuria/Glomerulonephritis
- Hypertension
- UTI
- Acute Kidney Injury
- Chronic Kidney Disease
- Anatomical/Congenital Abnormalities

- A 3 year old White male was seen in the clinic with peri-orbital and leg swelling. The vital signs are normal with BP of 95/60 mmHg. Serum electrolytes are normal.

Which of these will be of most help with making the diagnosis

A. Renal ultrasound
B. Echocardiogram
C. CBC
D. UA

- D

UA to check for proteinuria

# Proteinuria

- UA is a qualitative test
- Up/c < 0.2
- Abnormal: Up/c > 0.2
- Nephrotic Range:
  - > 3.5 g/24hrs/1.73 m2
  - > 40 mg/m2/hr
  - Up/c > 2

- A 6 year old boy presents with fever, URI symptoms. No gross hematuria. The vital signs are stable and BP is 102/62 mm Hg. UA demonstrates 1+ protein, and no blood, nitrites or LE.

- Of the following, the MOST likely cause for this patient's proteinuria is

A. Fever
B. HSP
C. Hemolytic uremic syndrome
D. Minimal change disease
E. Post-streptococcal glomerulonephritis

- A. Fever

# Transient Proteinuria

- Proteinuria is generally < 2+
- Causes:
  - Fever
  - Stress
  - Seizure
  - Dehydration
  - Cold exposure
  - Alkaline urine

# Etiologies of Proteinuria: Persistent

**Isolated Asymptomatic**

- Orthostatic

**Congenital or Acquired**

- Hydronephrosis
- Polycystic kidney disease
- Reflux nephropathy
- Renal dysplasia

**Secondary to Renal Disease**

**Idiopathic**

- Minimal change nephrotic syndrome
- Mesangial Proliferation
- Focal Segmental Glomerulosclerosis

**Secondary**

- Membranous Nephropathy
- Membranoproliferative Glomerulonephritis
- Post-infectious Glomerulonephritis
- Lupus glomerulonephritis
- Henoch-Schönlein purpura nephritis
- HIV-associated nephropathy

# Proteinuria - When to refer

- Persistent proteinuria
- Strong family history of renal disease
- Systemic findings
- Hypertension and/or edema
- Coexistence of hematuria with or without casts
- Increased serum creatinine
- Family anxiety

# Nephrotic Syndrome (NS)

- Heavy proteinuria
- Hypoalbuminemia
- Edema
- Hyperlipidemia

# Definition & Diagnosis of nephrotic syndrome

| | | |
|---|---|---|
| | 1. **Massive persistent proteinuria:** | 1000 mg/m2/day or > 40 mg/m2/hr<br>Up/c > 2.0 in spot urine sample<br>>3.5 g/day (adult),<br>>100 mg/kg/day or |
| | 2. **Hyoproteinemia:**<br>**or**<br>**Hypoalbuminemia:** | <5.5 g/dl<br><2.5 g/dl |
| | 3.**Hypercholesterolemia:** | >250 mg/dl (adult), >200 mg/dl (infant) |
| | 4. **Edema** | |

# Secondary Causes of NS

- Infection: HBV, HCV, HIV
- Medication: penicillamine, NSAIDS
- Malignancy: Hodgkin's lymphoma
- Immune disease: SLE

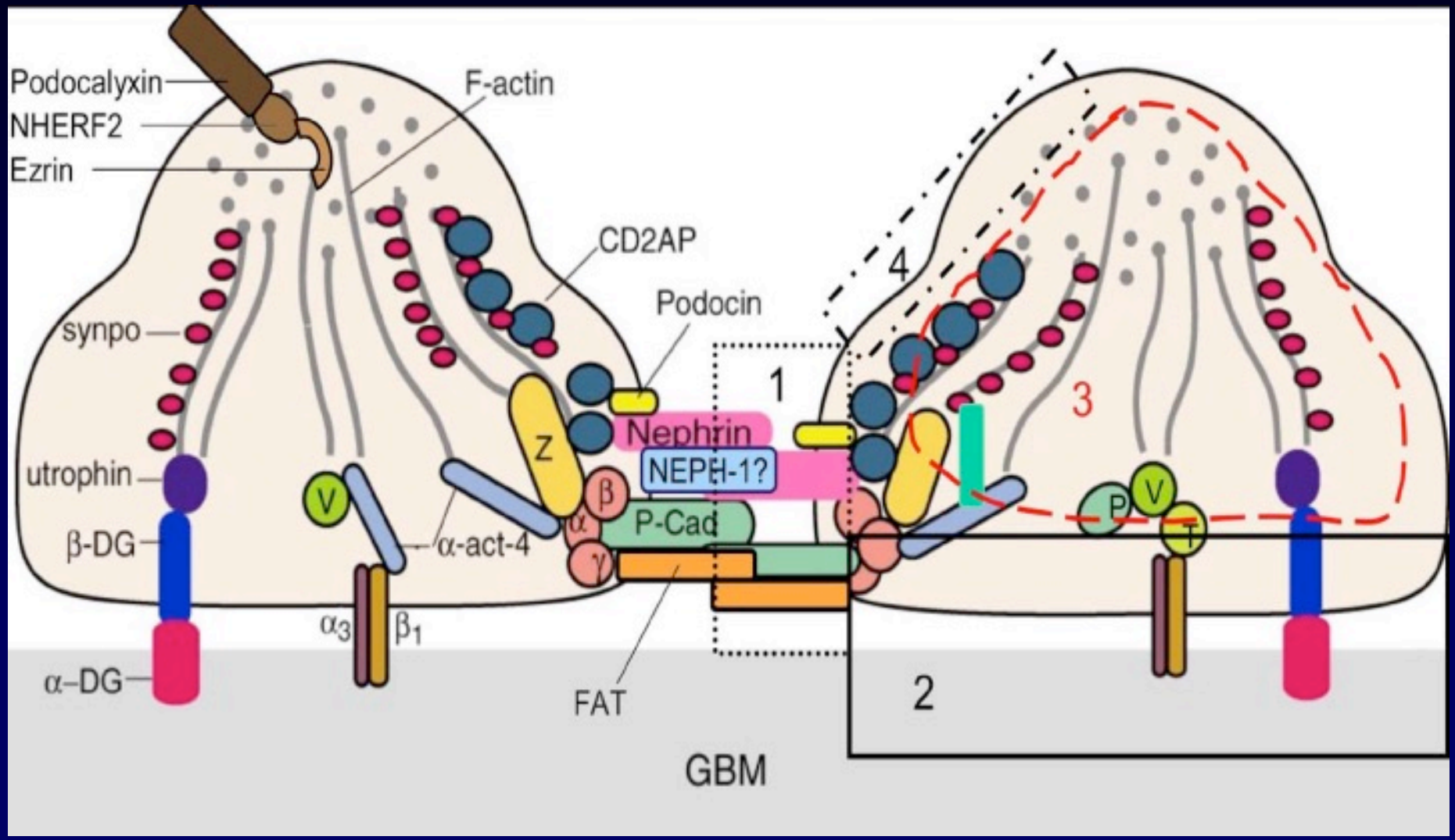
# Primary NS: Histological Classification

- Minimal change disease (MCNS)
- Mesangial proliferative glomerulonephritis
- Focal segmental glomerulosclerosis
- Membranoproliferative glomerulonephritis
- Membranous nephropathy

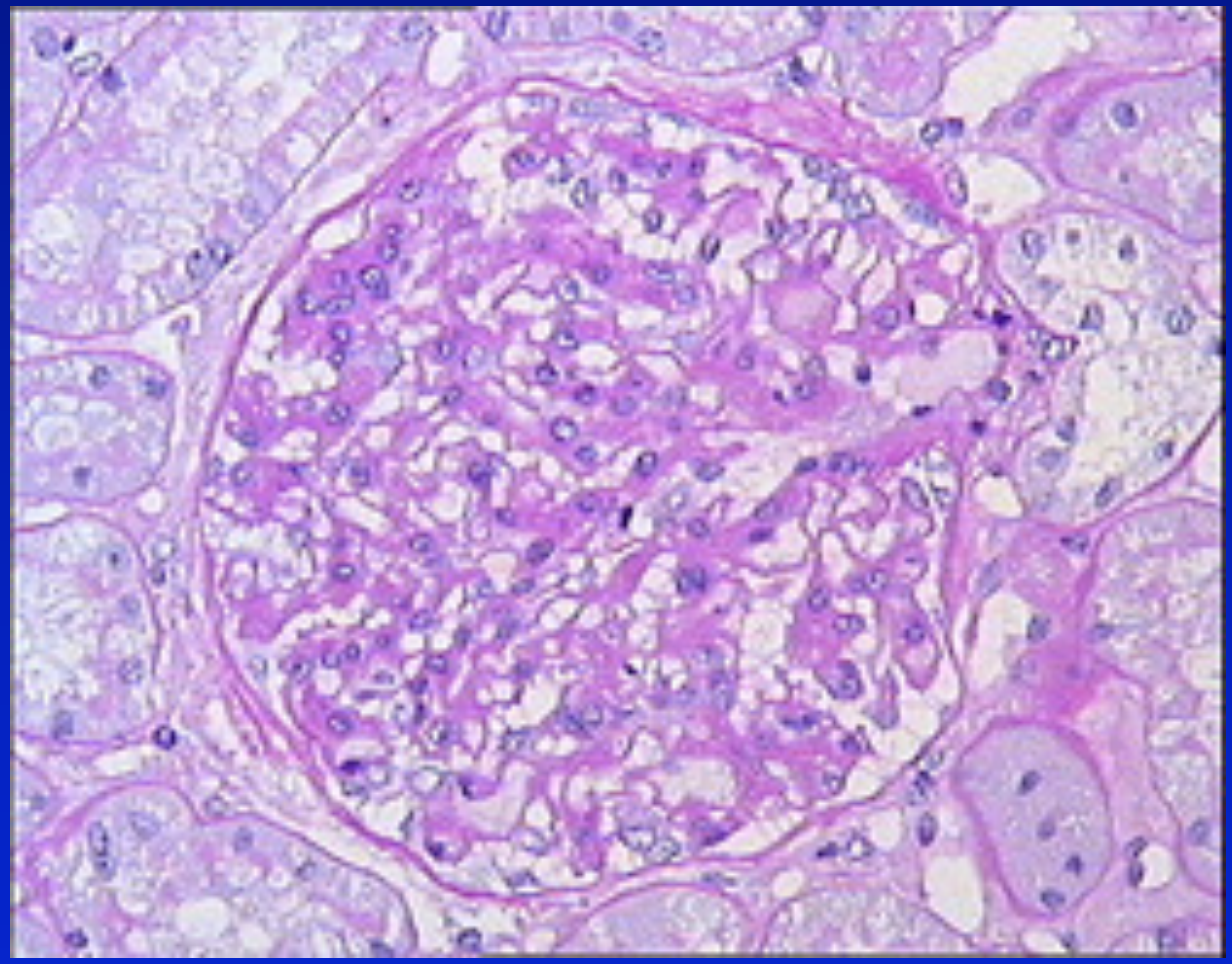
# Congenital/Infantile Nephrotic Syndrome

- Congenital - Most common type is Finnish type congenital NS
- Presents during first 3 months of life, autosomal recessive inheritance
  - Due to Nephrin mutation
- Infantile Nephrotic Syndrome: between 3 months and 12 months of age

# Molecular anatomy of foot processes

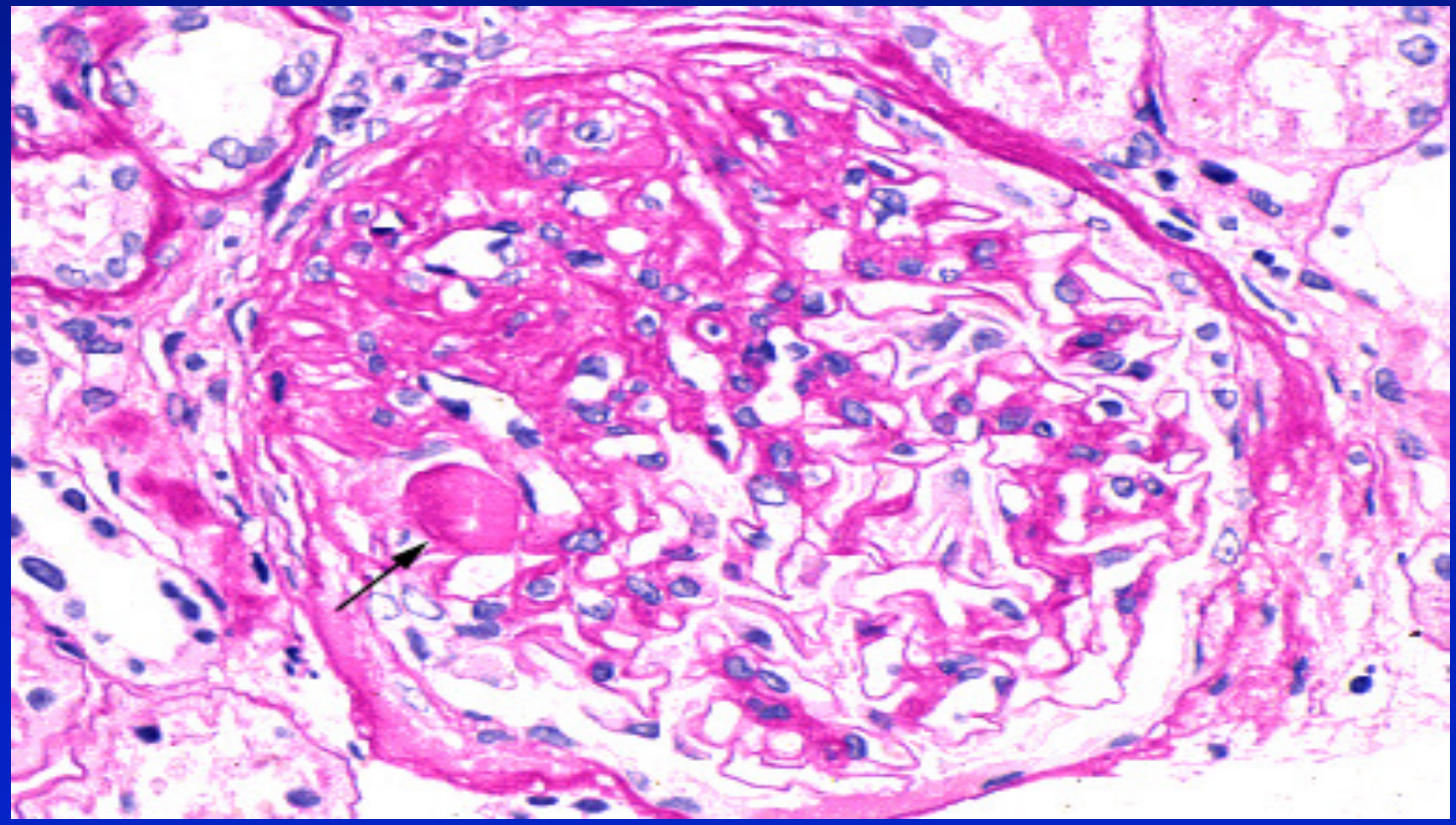


# Minimal Change Disease



Uptodate

# FSGS



Uptodate

# Treatment of NS

- Supportive

- Educate patient & family about the disease and side effects of medications
- Sodium restriction
- Decrease saturated fat
- Albumin infusion followed by IV Furosemide

- Specific

- Prednisone 60 mg/$m^2$/day for 4-6 weeks
- Then decrease to 40 mg/ $m^2$/day given QOD for 4-6 weeks.
- Then taper by 5 mg/ $m^2$ every 2 weeks until off

# Indication for Kidney Biopsy in NS

- Age of onset < 1 yr or > 10 yr
- Atypical features
  - gross hematuria
  - severe hypertension
  - persistent renal insufficiency
  - low C3
- Steroid resistant > 4 weeks
- Steroid dependent or frequent relapse

An 8-year-old boy presents with tea colored urine. He has very mild edema. The following workup should be done except.

A. Complement studies

B. BMP

C. Urinalysis for protein

D. Monitor blood pressure and urine output

E. Obtain CT scan

- E. Obtain a CT scan

# Types of Hematuria

- Gross Hematuria
- Microscopic Hematuria
  1. Microscopic hematuria with clinical symptoms
  2. Asymptomatic microscopic (isolated) hematuria
  3. Asymptomatic microscopic hematuria with proteinuria.

# Hematuria- Laboratory Evaluation

-UA

-Urine culture

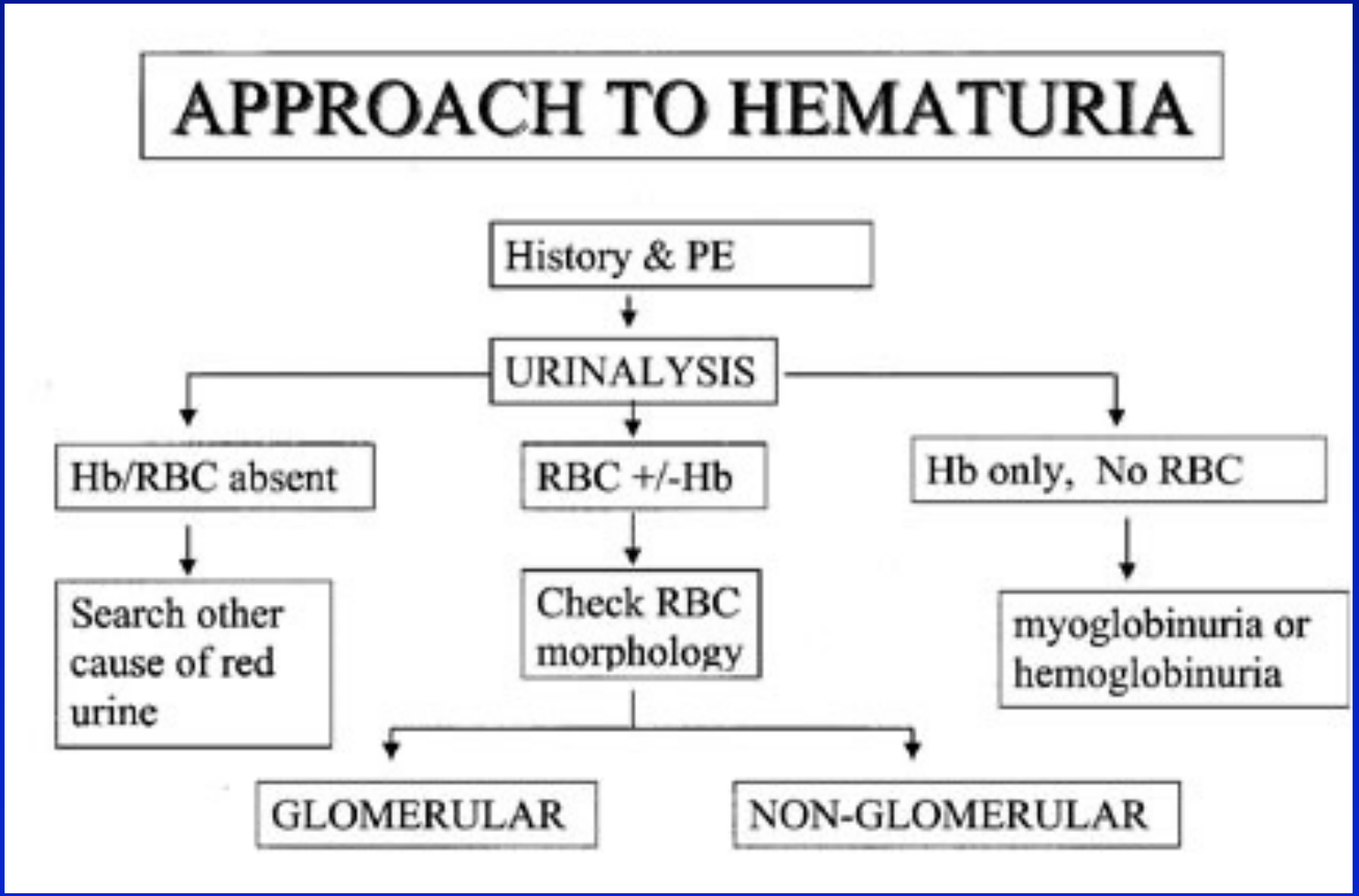
-Up/c

-(Uca/cr)

-C3, ASO, BUN/Creatinine

-Renal/Bladder ultrasound

# Initial Evaluation



# When to Refer for Hematuria

- Strong family history of renal disease and/or nerve deafness
- Recurrent gross hematuria
- Hematuria with proteinuria
- Systemic complaints
- Abnormal renal function (creatinine)
- Family anxiety

# Thin Basement Membrane Disease

-It is a diagnoses of exclusion

-Autosomal dominant

-Renal Biopsy: mild mesangial hypercellularity and thinning of the glomerular basement membrane on EM.

# IgA Nephropathy

- Most common glomerulonephritis in the world
- Very low rates in blacks
- Microscopic hematuria
- Intermittent gross hematuria associated with URI
- Wide range of proteinuria from mild to heavy
- Deposition of IgA in the mesangium
- Long term prognosis is usually good

# Henoch- Schonlein Purpura (HSP)

- Exact cause is unknown
- Multisystem involvement: skin, joints, GI and kidneys
- IgA deposition in the mesangium
- Most common systemic vasculitis of childhood
- 75% from 2-11 years; peak age 5 y/o
- Microscopic hematuria +/- gross hematuria
- Kidney involvement may occur at the same time or few weeks after the extra-renal involvement
- Weekly UA to monitor for hematuria/proteinuria

# Alports Syndrome

- Eye abnormalities, high frequency sensorineural hearing loss, hereditary nephritis
- X-linked (85%), autosomal recessive, autosomal dominant
- Persistent microhematuria, recurrent macroscopic hematuria,
- Progressive proteinuria, deteriorating GFR and progression to ESRD
- Mutations in Type-IV collagen

# Post Infectious Acute Glomerulonephritis

- Mostly due to grp A beta-hemolytic strep
- May follow throat or skin infection 2 to 4 weeks after
- Gross hematuria (tea/cola-colored urine)
- HTN, proteinuria, RCC, increase in creatinine
- Symptomatic management
- Self limiting
- Persistent microscopic hematuria
- The depressed C3 normalize by 6 to 8 weeks

- A 6 year old boy is seen for routine assessment. BP is 106/60 mm Hg. Physical examination is normal
- UA shows: 3+ blood, negative for protein, nitrite and LE, 10 to 20 RBC/hpf,
- The mother has a history of microscopic hematuria and three maternal uncles required dialysis between 14 and 16 years of age.
- Of the following, the MOST likely cause for this patient's urinary findings is

A. ADPKD
B. Alports nephritis
C. ARPKD
D. Post infectious acute glomerulonephritis
E. Thin glomerular basement disease

- B. Alports Nephritis

- A 16-year old boy presents with pain in the lower extremities and reddish urine. He has been jogging and lifting weight excessively.
- Urine test strip: 3+ blood, no protein, otherwise negative
- Microscopy: Less than 5 RBC/HPF, less than 5 WBC/HPF, no crystals
- Of the following, the MOST likely diagnosis in this boy is

A. Hemoglobinuria
B. Kidney stones
C. Hypercalciuria
D. IgA nephropathy
E. Myoglobinuria

- E. Myoglobinuria

CLINICAL PRACTICE GUIDELINE Guidance for the Clinician in Rendering Pediatric Care

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

# Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents

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# NEW Definitions for HTN

**TABLE 3** Updated Definitions of BP Categories and Stages

| For Children Aged 1–13 y | For Children Aged ≥13 y |
|---|---|
| Normal BP: <90th percentile | Normal BP: <120/<80 mm Hg |
| Elevated BP: ≥90th percentile to <95th percentile or 120/80 mm Hg to <95th percentile (whichever is lower) | Elevated BP: 120/<80 to 129/<80 mm Hg |
| Stage 1 HTN: ≥95th percentile to <95th percentile + 12 mmHg, or 130/80 to 139/89 mm Hg (whichever is lower) | Stage 1 HTN: 130/80 to 139/89 mm Hg |
| Stage 2 HTN: ≥95th percentile + 12 mm Hg, or ≥140/90 mm Hg (whichever is lower) | Stage 2 HTN: ≥140/90 mm Hg |

# New BP Tables

TABLE 4 BP Levels for Boys by Age and Height Percentile

| Age (y) | BP Percentile | SBP (mm Hg) | | | | | | | DBP (mm Hg) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Height Percentile or Measured Height | | | | | | | Height Percentile or Measured Height | | | | | | |
| | | 5% | 10% | 25% | 50% | 75% | 90% | 95% | 5% | 10% | 25% | 50% | 75% | 90% | 95% |
| 8 | Height (in) | 47.6 | 48.4 | 49.8 | 51.4 | | | | | | | | | | |
| | Height (cm) | 121 | 123 | 126.5 | 130.6 | | | | | | | | | | |
| | 50th | 93 | 94 | 95 | 97 | | | | | | | | | | |
| | 90th | 107 | 107 | 108 | 110 | | | | | | | | | | |
| | 95th | 110 | 111 | 112 | 113 | | | | | | | | | | |
| | 95th + 12 mm Hg | 122 | 123 | 124 | 125 | | | | | | | | | | |
| | 95th + 12 mm Hg | 119 | 120 | 121 | 121 | 122 | 123 | 124 | 78 | 79 | 80 | 81 | 82 | 82 | 83 |
| 6 | Height (in) | 43.4 | 44.2 | 45.4 | 46.8 | 48.2 | 49.4 | 50.2 | 43.4 | 44.2 | 45.4 | 46.8 | 48.2 | 49.4 | 50.2 |
| | Height (cm) | 110.3 | 112.2 | 115.3 | 118.9 | 122.4 | 125.6 | 127.5 | 110.3 | 112.2 | 115.3 | 118.9 | 122.4 | 125.6 | 127.5 |
| | 50th | 93 | 93 | 94 | 95 | 96 | 97 | 98 | 54 | 54 | 55 | 56 | 57 | 57 | 58 |
| | 90th | 105 | 105 | 106 | 107 | 109 | 110 | 110 | 68 | 68 | 67 | 68 | 68 | 69 | 69 |
| | 95th | 108 | 109 | 110 | 111 | 112 | 113 | 114 | 69 | 70 | 70 | 71 | 72 | 72 | 73 |
| | 95th + 12 mm Hg | 120 | 121 | 122 | 123 | 124 | 125 | 126 | 81 | 82 | 82 | 83 | 84 | 84 | 85 |
| 7 | Height (in) | 45.7 | 46.5 | 47.8 | 49.3 | 50.8 | 52.1 | 52.9 | 45.7 | 46.5 | 47.8 | 49.3 | 50.8 | 52.1 | 52.9 |
| | Height (cm) | 116.1 | 118 | 121.4 | 125.1 | 128.9 | 132.4 | 134.5 | 116.1 | 118 | 121.4 | 125.1 | 128.9 | 132.4 | 134.5 |
| | 50th | 94 | 94 | 95 | 97 | 98 | 98 | 99 | 56 | 56 | 57 | 58 | 58 | 59 | 59 |
| | 90th | 106 | 107 | 108 | 109 | 110 | 111 | 111 | 68 | 68 | 69 | 70 | 70 | 71 | 71 |
| | 95th | 110 | 110 | 111 | 112 | 114 | 115 | 116 | 71 | 71 | 72 | 73 | 73 | 74 | 74 |
| | 95th + 12 mm Hg | 122 | 122 | 123 | 124 | 126 | 127 | 128 | 83 | 83 | 84 | 85 | 85 | 86 | 86 |

# Hypertension

- A secondary cause is more likely to be found the younger the patient  and the higher the BP
- Renal diseases are the most common causes of secondary HTN
- Complete history and P.E
- ABPM is the measurement of BP values over a 24-hour period preferably at home

  - May be used to assess for “White Coat Syndrome”

# Hypertension - Workup

- BMP: to evaluate the  electrolytes, creatinine
- CBC
- UA: hematuria, proteinuria
- Echocardiogram: LVH
- Renal sonogram: anatomical anomalies

# Hypertension - Treatment

- Prehypertension: Lifestyle modifications
- Stage 1 without target organ damage: lifestyle modifications. Start medication if is not decreased in 4 to 6 months
- Stage 1 with symptoms or target organ damage: lifestyle modifications + medications
- Stage 2: start medications
- Secondary HTN: treat the cause

# HTN: Non-pharmacologic therapy

- Sodium restriction
- Exercise
- Weight loss where appropriate
- Avoidance of pressor substances (caffein, pseudoephedrine)
- Stress reduction

# How to select appropriate therapy?

- Always try to approach the mechanism of hypertension
- Start with single agent and increase dose as tolerated
- A second medication may be introduced if needed
- Monitor closely for side effects
- Evaluate non-compliance in refractory cases

# ORAL AGENTS FOR HYPERTENSION

- Diuretics (Loop, Thiazides)
- Vasodilators (Hydralazine, Minoxidil)
- ACEi (Captopril, Enalapril)
- ARB (Candesartan, Losartan)
- Calcium Channel Blockers (Amlodipine, Nifedipine)
- Alpha/Beta Blockers (labetalol)
- Beta Blockers (propranolol)
- Alpha blockers (Prazosin)
- Central Agents (clonidine)

- A 12-year-old girl presented for follow up of a previously elevated BP reading. She has no symptoms. Her weight is above the 99$^{th}$ percentile and her vital signs are stable. The SBP and DBP are between the 90$^{th}$ and 95$^{th}$ percentile for age and height. Physical examination findings are normal.
- Of the following, the MOST appropriate next step is to

A. Initiate ACEi or ARB
B. Check for TSH, Free T4
C. Increase physical activity and modification of diet
D. Obtain serum catecholamine level
E. Initiate calcium channel blocker

- C. Increase physical activities and modification of diet

- An 8 year old male is followed by the pediatrician for the past 2 to 3 weeks with elevated BP.
- The boy has had 4 episodes of pyelonephritis. His BP is 142/86 mm Hg and the rest of the vital signs are stable. Multiple BP readings show values elevated values
- Sonogram shows the left kidney to be 8 cm and the right kidney to be 4 cm.
- Of the following the MOST likely cause for this patient's elevated blood pressure

A. Renal scarring from prior pyelonephritis
B. Essential hypertension
C. Renal artery stenosis
D. Coarctation of the aorta
E. ADPKD

- A. Renal scarring from prior pyelonephritis

# UTI

- A 1.5 year old girl is diagnosed with the first febrile UTI. She is not eating well. UA shows pyuria and bacteria. Urine culture is obtained. Antibiotics are given How to proceed?
  - What are some of your concerns?
  - Radiographic follow-up
  - Long-term monitoring

# Common Organisms Causing UTIs

- Enterobacteriaceae most common
  - Of these, E coli causes approximately 80% of UTIs
  - Others include Klebsiella, Enterobacter, Citrobacter, Proteus, etc.
- Staphylococcus and Enterococcus are most common gram positives

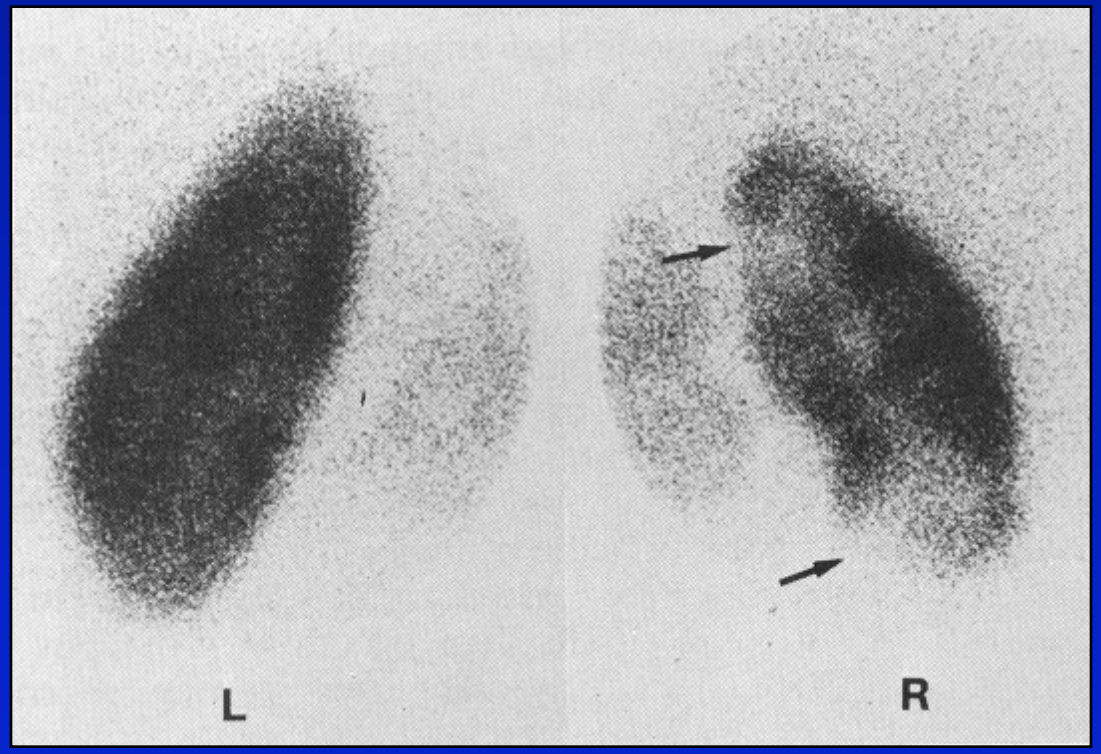
# Risk Factors for Kidney Damage from UTI

- Young age, especially < 1 yr
- Delay in initiating effective antibacterial therapy for acute pyelonephritis
- Anatomic or neurogenic obstruction
- Severe reflux (dilated collecting system)
- Recurrent episodes of acute clinical pyelonephritis

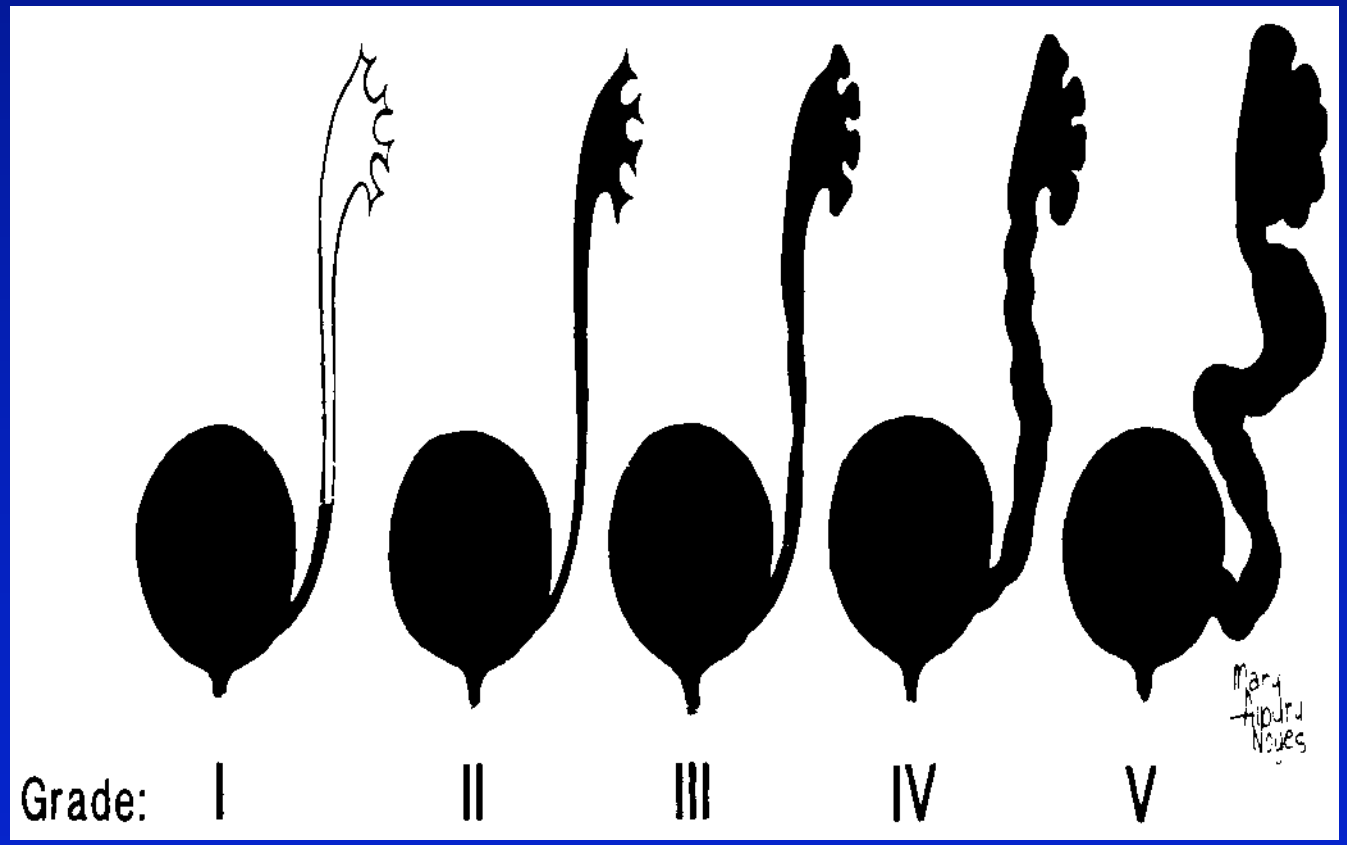
# UTI - Evaluation

- Renal Sonogram
- VCUG: for evaluation of vesico-ureteral reflux
- Renal Scan
  - DMSA Scan: scarring
  - MAG-3: obstruction
- Vesico-ureteral Reflux
  - Prophylactic antibiotics
  - Ureteral re-implantation
  - Deflux

# Defective Uptake of DMSA in Acute Pyelonephritis



# Grades of Reflux



- A 13 year old girl presents with symptoms of dysuria and left flank pain. Her temperature is 102 F. You can elicit CVT. Her UA: 2+ blood, 1+ protein, 3+ LE, + nitrite, 10 RBC/HPF, 4+ bacteria
- Of the following, the MOST likely diagnosis is

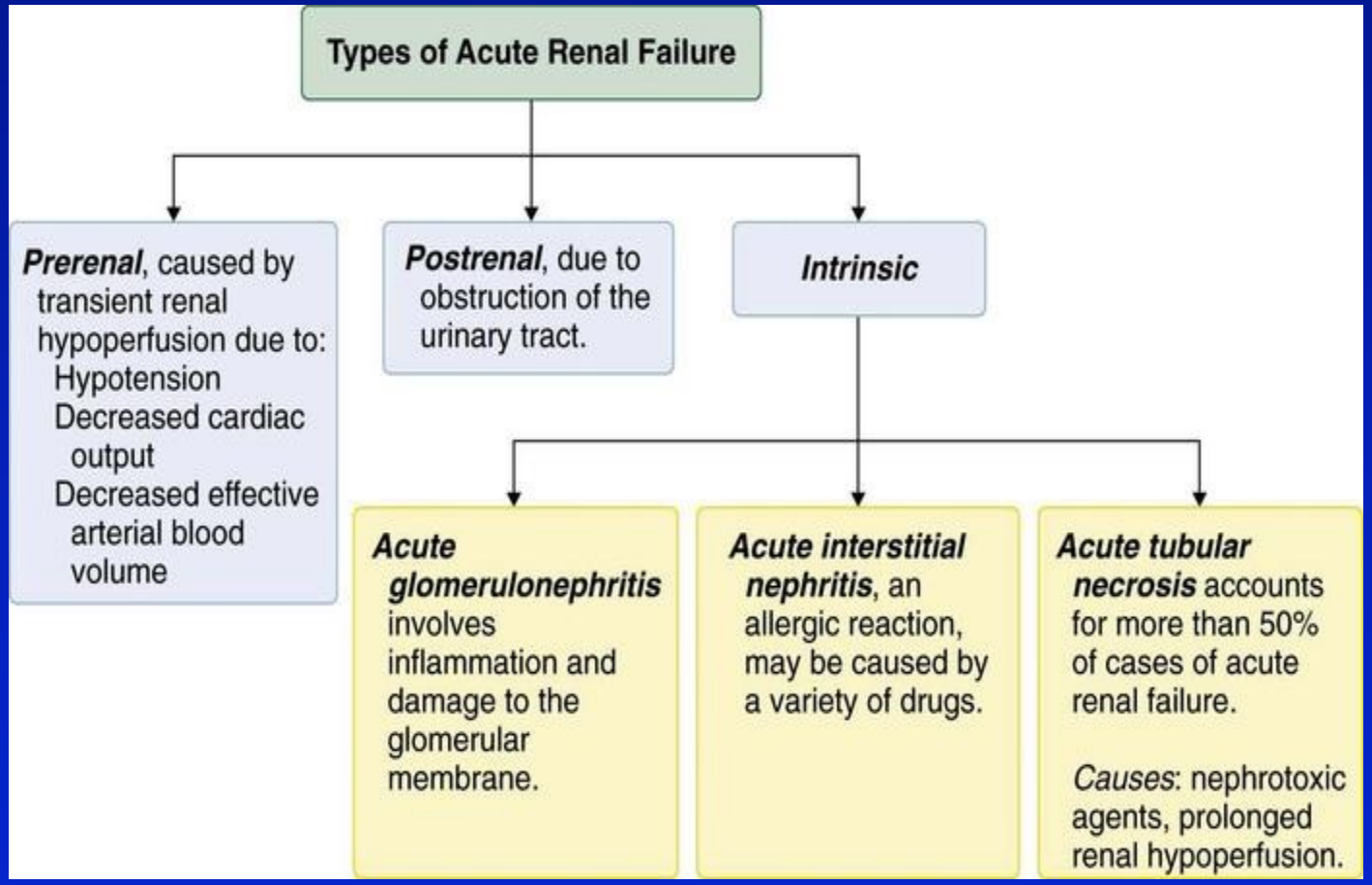
A. Acute bacterial cystitis
B. Acute glomerulonephritis
C. Acute pyelonephritis
D. Bacterial urethritis
E. Nephrolithiasis

- C. Acute pyelonephritis

# Acute Kidney Injury (AKI)

- Loss of renal function over a period of hours to days
- Abrupt decrease in glomerular filtration rate
- Retention of urea, creatinine and other waste products
- Inability to regulate fluid and electrolyte homeostasis appropriately
- Oliguria may or may not be present.

# Etiology of AKI




Atlas of Kidney Disease

# AKI: Evaluation

- BMP: BUN, creatinine, K
- EKG
- UA, Urine electrolytes
- Renal ultrasound
- Specific blood tests based on underlying condition

# AKI
# Supportive Management

1. Initial management
2. Fluid management
3. Electrolyte abnormalities
4. Diuretics Rx
5. Medication adjustment
6. Nutrition management
7. RRT if indicated

# AKI
# Supportive Management

- Potassium
  - Diet restriction
  - Kayexalate
  - Insulin and glucose
- Blood pressure
  - IV/PO meds
- Fluid Overload
  - Na restriction
  - Furosemide

# AKI: Indications for Dialysis

- Refractory hyperkalemia
- Refractory hypertension
- Symptomatic ECF volume overload
- Symptomatic azotemia
  - Infection
  - Bleeding
  - CNS changes

# Chronic Kidney Disease

- Chronic renal failure is present when the GFR is permanently decreased
- Kidney damage for $\geq$ 3 months
- Loss of functional nephron population
- Elevation of serum creatinine

# Stages of Chronic Kidney Disease[18]

| Description | Stage | GFR (mL/min/1.73 m²) |
|---|---|---|
| Kidney damage with normal or high GFR | 1 | ≥ 90 |
| Kidney damage with mild decrease in GFR | 2 | 60-89 |
| Moderate decrease in GFR | 3 | 30-59 |
| Severe decrease in GFR | 4 | 15-29 |
| Kidney failure | 5 | < 15 (or dialysis) |

# CKD: Causes

- Non-glomerular
  - Hypoplasia/dysplasia
  - Reflux nephropathy
  - Obstructive uropathy
    - PUV
    - Prune Belly
    - Neurogenic bladder

# CKD: Causes

- Glomerular
  - FSGS
  - HUS
  - SLE
  - Membranoproliferative MPGN)
  - Alport
  - IgA Nephropathy
  - Membranous nephropathy
  - NOT diabetic or hypertensive nephropathy

# CKD: Clinical manifestations

- Growth failure
- Hypertension
- Electrolyte abnormalities
  - Hyperkalemia, Hypocalcemia, Metabolic acidosis
- Edema
- Signs of underlying disease
- Anemia

# CKD: Diagnosis

- Renal sonogram
- Blood tests
  - C3, C4, CH50
  - ASLO
  - ANA, dsDNA, Ro, La, Sm
  - ANCA
  - Anti-GBM
  - Renal biopsy

# CKD: Management

- Nutritional supplementations
- Electrolyte abnormalities
- Protein restriction
  - Impact on growth
  - Effect in more advanced CKD
- BP control
  - Disease progression
  - ACEI/ARB

# CKD: Management

- Endocrine treatments
  - Growth hormone
    - To improve growth
  - Erythropoietin
    - Corrects the anemia
  - Calcitriol
    - Vit D analogue
    - Helps to correct the bone disease

- A 7 year old male presents with increased tiredness for the past several months. The reminder of the history is unremarkable. His weight is at the 10$^{th}$ %, height is by the 5$^{th}$ %. Vital signs are stable. UA findings are unremarkable.
- Other lab results are: Na 138, K 5.6, Cl 98, HCO3 13, BUN 78, Creatinine 7.8
- Of the following, the MOST likely additional finding expected for this child is

A. Enlarged kidneys on ultrasonography
B. Metabolic alkalosis
C. Increased PTH level
D. Thrombocytopenia
E. Reticulocytosis

- C. Increased PTH level

- An 8 year old boy presents for routine health assessment. He has FTT with his height and weight below the 5th percentile for age. Laboratory evaluation reveals: creatinine, 3.0 mg/dL; blood urea nitrogen, 40 mg/dL; calcium, 8.0 mg/dL; phosphorus, 7.5 mg/dL; and intact parathyroid hormone, 850 pg/mL
- Of the following, the MOST likely cause of the hypocalcemia in this boy is

- A. Nutritional vitamin D deficiency
- B. Primary hyperparathyroidism
- C. Liddle syndrome
- D. Renal osteodystrophy
- E. Fanconi syndrome

- D. Renal osteodystrophy

# Autosomal recessive polycystic kidney disease (ARPKD)

- Mutations of PKHD1 (in chromosome 6)
- Affects 1 in 20,000
- Age of presentation varies
- Associated oligohydramnios
- Liver involvement universal
  - Caroli disease (intrahepatic bile duct dilatation)
- Kidneys are large
- Decrease in GFR
- Hypertension

# ARPKD: Management

- Control BP
- Treat liver disease
- Combined liver-kidney transplant

# Autosomal dominant polycystic kidney disease (ADPKD)

- Mutations of PKD1 (85%) in chromosome 16 and PKD2 in chromosome 4
- Affects 1 in 1000
- Hypertension
- Cysts in other organs: liver, pancreas, ovaries
- Cerebral aneurysms
- Complications of the renal cysts- pain, infection, rupture, kidney stone
- Cannot be excluded (by ultrasound) until the $4^{th}$ decade of life

# ADPKD: Management

- BP management
- Avoid OTC cold remedies, caffeine
- Use of ACEI
- Tyrosine kinase inhibitors, somatostatin

- A newborn male has wrinking of the abdominal wall skin. There was history of oligohydramnios during pregnancy.

- Of the following, the MOST likely additional findings expected in this infant are cryptorchidism and

A. Bilateral hydronephrosis
B. Hypospadias
C. Epispadias
D. Medullary cystic kidneys
E. Multicystic dysplastic kidney

- A. Bilateral hydronephrosis

# THANK YOU
# AND
# GOOD LUCK