PEDIATRIC UPDATE ON HYPERTENSION AND RENAL FAILURE

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Objectives

- To review background of pediatric hypertension
- To learn about ambulatory BP monitoring
- To discuss the HTN Best Practice Alert protocol at KP
- To review definitions of acute kidney injury and chronic kidney disease

Background

- NHANES (National Health and Nutrition Examination Surveys) data from 2003–2006:
- 13.6% of the boys aged 8–17 years and 5.7% of the girls aged 8–17 years were classified as having pre-hypertension
- 2.6% of the boys aged 8–17 and 3.4% of the girls aged 8–17 were classified as having hypertension
- Non-Hispanic black girls were more likely to be classified as having pre-hypertension when compared with non-Hispanic white girls (odds ratio=1.53)

Reference: Yechiam O et al. American Journal of Hypertension, 2009.

MEASUREMENT OF BP IN CHILDREN

- Children > 3 years old who are seen in a medical setting should have their BP measured.
- The preferred method of BP measurement is auscultation.
- Correct measurement requires a cuff that is appropriate to the size of the child's upper arm.
- Elevated BP must be confirmed on 3 occasions before characterizing a child as having HTN.
- Measures obtained by oscillometric devices that exceed the 90% should be repeated by auscultation

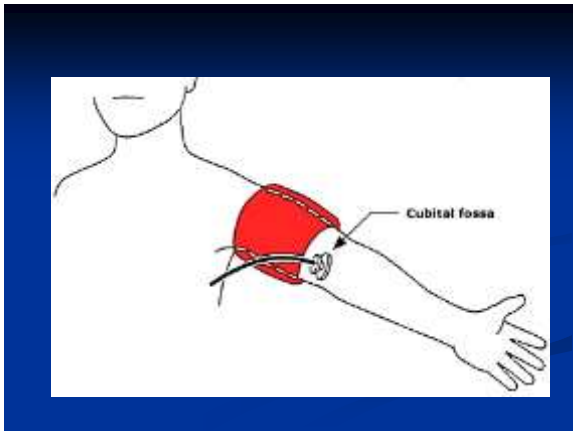
< 3 YEARS OLD

TABLE 1. Conditions Under Which Children <3 Years Old Should Have BP Measured

History of prematurity, very low birth weight, or other neonatal complication requiring intensive care
Congenital heart disease (repaired or nonrepaired)
Recurrent urinary tract infections, hematuria, or proteinuria
Known renal disease or urologic malformations
Family history of congenital renal disease
Solid-organ transplant
Malignancy or bone marrow transplant
Treatment with drugs known to raise BP
Other systemic illnesses associated with hypertension (neurofibromatosis, tuberous sclerosis, etc)
Evidence of elevated intracranial pressure

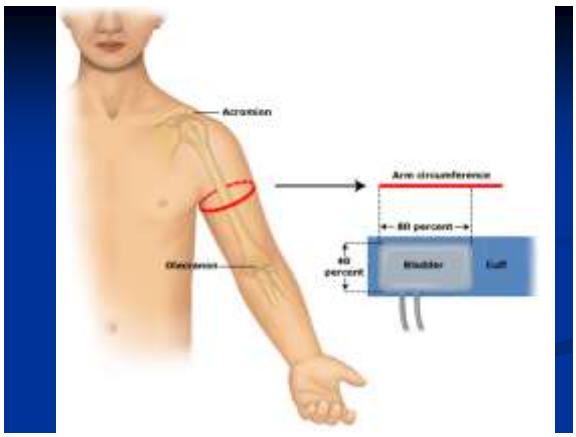
BP measurement

- Place stethoscope over the brachial artery pulse, proximal and medial to the cubital fossa, and below the bottom edge of the cuff (ie, ~2cm above the cubital fossa)
- Child should have avoided stimulant drugs or foods
- Child should have been sitting quietly for 5 minutes with his or her back supported, feet on the floor and right arm supported, cubital fossa at heart level



BP CUFF

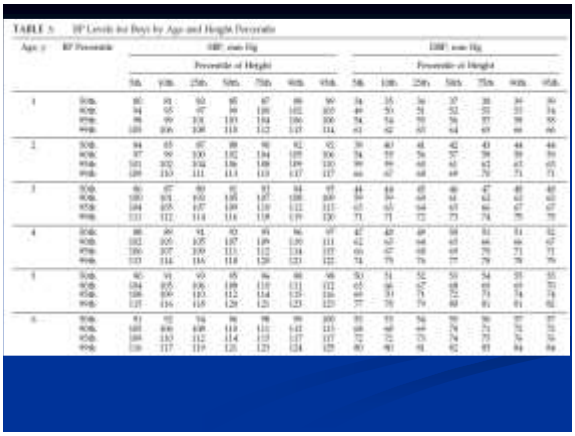
- Bladder width >40% of arm circumference at a point between the olecranon and the acromion.
- Cuff bladder length should over 80-100% of the circumference of the arm.
- Standard cuff dimensions for children should be adopted.



Pediatric Hypertension: Definition (revised in 2017)

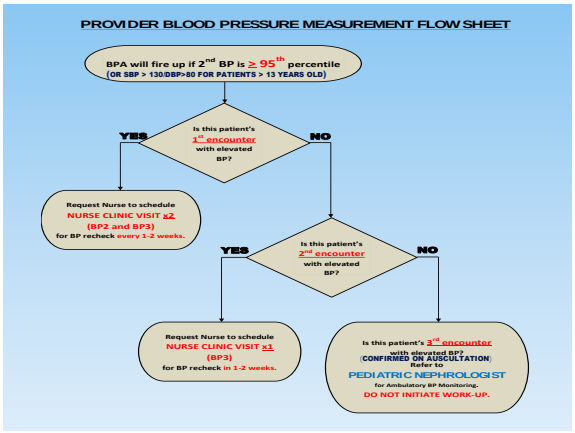
Children 3-12 y/o	Children ≥ 13 y/o
Normal BP: <90th percentile	**Normal** BP: <120/<80
Elevated BP: ≥90th -<95th or 120/80 whichever is lower	**Elevated** BP:120/<80-129/<80
Stage 1 HTN: ≥95th-<95th+12 mm Hg or 130/80-139/89 whichever is lower	**Stage 1** HTN: 130/80-139/89
Stage 2 HTN: ≥95th+12 mm Hg, or ≥ 140/90	**Stage 2** HTN: ≥ 140/90

Flynn et al, Ped Sept 2017



Using HealthConnect

- To determine patient's BP %ile based on gender, height and age, type in smartphrase ***.BPFAW95***
- To look up past blood pressure values, type in ***.lastbp3*** or ***.lastbp[#***



At Peds Nephrology Consult

- If patient is asymptomatic, we will recommended ABPM to rule out white coat hypertension before proceeding with additional work up
- If ABPM confirms HTN, we will obtain additional work up, including renal ultrasound, laboratory tests and echocardiogram to rule out LVH
- We will determine if patient needs pharmacologic agent *vs.* continuing lifestyle management based on ABPM result

What is ABPM?

Ambulatory BP Monitoring (ABPM)

- Portable automated BP device that takes reading every 15-30 minutes when awake and every 30-60 min when asleep.
- BP follows a circadian pattern, falling by 13-20% below daytime levels during sleep at night ("nocturnal dipping").
- BP load in children is defined as percentage of BP > 95% on ABPM.
- High BP load and the absence of nocturnal dipping have been associated with end-organ damage in both adults and children.

Sorof, JM et al. Hypertension 2002; 39:903.

Ambulatory BP Monitoring (ABPM)

ABPM is used for evaluation of:

- White coat hypertension
- Hypotensive symptoms
- Masked hypertension
- Effectiveness of antihypertensive treatment
- BP pattern in patients with chronic kidney disease, diabetes, autonomic dysfunction or episodic hypertension

Patient has true hypertension if…

- …> 25% of BP loads exceeds 95%ile or greater
- …< 10% dip during nocturnal BP measurements

Etiology of HTN

- Newborn
- Toddler
- Older kids
- Adolescents

ETIOLOGY BY AGE

- Newborn
  - Renal artery thrombosis
  - Renal vein thrombosis
  - Congenital renal malformation
  - Coarctation
  - Renal artery stenosis
  - Bronchopulmonary dysplasia
- Infancy to 6 yr
  - Renal parenchymal disease
  - Renal artery stenosis
  - Coarctation
  - Medication
  - Endocrine
- 6-10 yr
  - Renal parenchymal disease
  - Renal artery stenosis
  - Essential hypertension
  - Endocrine causes
- Adolescence
  - Essential HTN
  - White-coat HTN
  - Renal parenchymal disease
  - Substance abuse
  - Endocrine causes

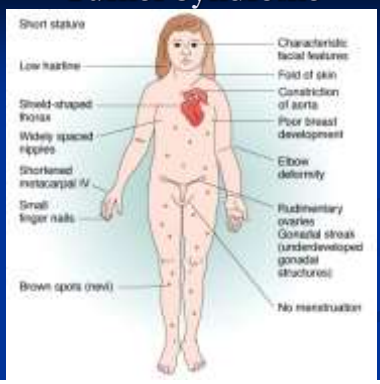
History

- History of hypertension
- Stopped using antihypertensive medications?
- Umbilical vessel catheterization
- Genitourinary abnormalities
- Recent head injury
- Medication history (steroids, OCP's, tacrolimus)
- Substance abuse
- Vision changes
- Headaches
- Confusion
- Somnolence
- Seizures
- Chest pain
- Respiratory difficulties
- Nausea or vomiting
- Oliguria

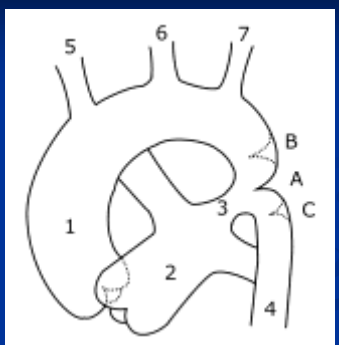
Physical Exam

- Vital signs and 4 limb blood pressures
- Fundoscopic exam – papilledema, hemorrhages
- Full neurologic exam
- Lungs – pulmonary edema
- CV – gallops
- Abdomen – hepatomegaly
- Extremities – edema, femoral pulses

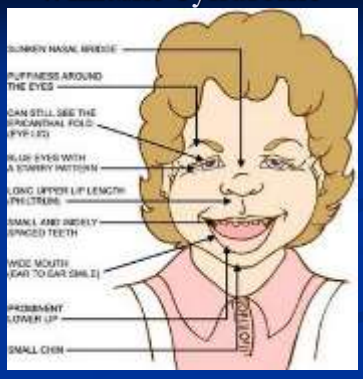
Turner Syndrome



Coarctation

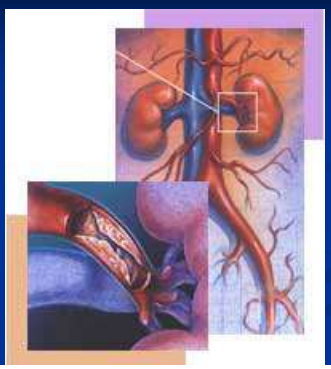


Williams Syndrome



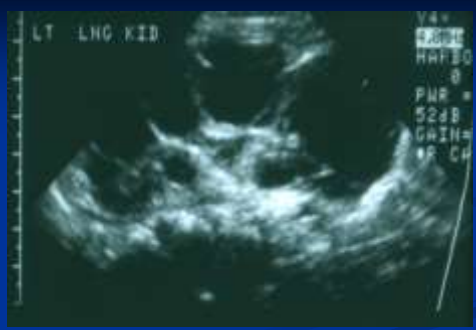
Neurofibromatosis

Renal Artery Stenosis



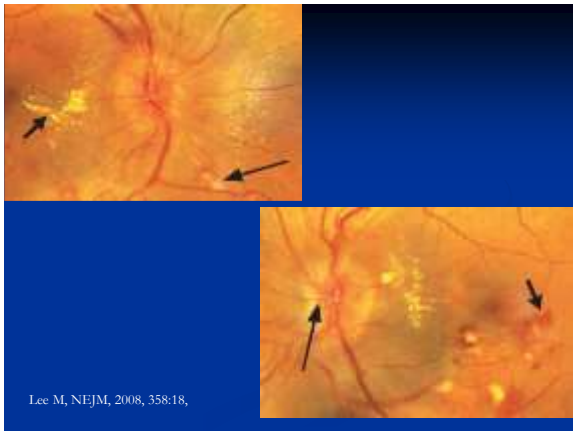
Tuberous Sclerosis

Head	Angiofibroma
Finger	Periungual fibroma
Skin	Hypomelanotic macules
Skin	Shagreen patch
Brain	Cortical Tuber
Brain	Subependymal nodule
Brain	astrocytoma
Eye	Retinal hamartoma
Heart	Rhabdomyoma
Lungs	Lymphangioleiomyomatosis
Kidneys	Angiomyolipoma



COMPLICATIONS OF HTN

- CNS
  - Hypertensive Encephalopathy
  - Retinopathy
- Cardiac
  - LVH
- Renal
  - Hypertensive nephropathy



Lee M, NEJM, 2008, 358:18,

PRES

TREATMENT

- Lifestyle modification:
  - Dietary changes – sodium restriction, increased fruits and vegetable and fiber
  - Increase physical activity
  - Weight loss in the obese
- Pharmacologic agents
  - If mild, may wait for work up
  - If severe, control with antihypertensives while undergoing work up

Sodium restriction in HTN

- Sodium reduction in children and adolescents has been associated with BP reduction in the range of 1-3mm Hg.
- Daily sodium recommendations is only 1.2 g/day for 4- to 8-year-olds and 1.5 g/day for older children.

Exercise and Obesity

- Regular aerobic activities (30-60 minutes of moderate physical activity on most days) and limitation of sedentary activities to <2 hours per day
- With the exception of power lifting, resistance training is also helpful
- Competitive sports participation should be limited only in the presence of uncontrolled stage 2 hypertension

TREATMENT

TABLE 6. Indications for Antihypertensive Drug Therapy in Children

Symptomatic hypertension
Secondary hypertension
Hypertensive target-organ damage
Diabetes (types 1 and 2)
Persistent hypertension despite nonpharmacologic measures

ACE-I/ARBs

ACE Is	
Captopril (Capoten, generic)	Newborns: 0.1–0.4 mg/kg/day ÷ Q8–12 h Infants: 0.15–0.30 mg/kg/dose and children 0.30–0.50 mg/kg/dose t.i.d.–q.i.d. Maximum 450 mg/day
Benazepril (Lotensin, generic)	0.2–0.6 mg/kg/day, given once daily Maximum 40 mg/day
Enalapril (Vasotec, generic)	0.08–0.60 mg/kg/day daily or ÷ Q12 h Maximum 40 mg/day
Lisinopril (Prinivil, Zestril, generic)	0.07–0.60 mg/kg/day, given once daily Maximum 40 mg/day
ARBs	
Irbesartan (Avapro)	6–12 years: 75–150 mg/day, given once daily >13 years: 150–300 mg/day given once daily
Losartan (Cozaar)	0.75–1.44 mg/kg/day given once daily. Maximum 100 mg/day

Note: ACE-I causes coughing. Avoid in single kidney with renal artery stenosis and pregnancy.

β-blockers

β-blockers	
Atenolol (Tenormin, generic)	0.5–2.0 mg/kg/day ÷ Q12 h Maximum dose 100 mg/day
Propranolol (HCl) (Inderal, generic)	0.5–4 mg/kg/day ÷ Q12–6 h Maximum 640 mg daily
Propranolol ER (Inderal LA, InnoPran XL)	1–4 mg/kg/day given once daily Maximum 640 mg daily
Metoprolol (Lopressor, Toprol XL, generic)	1–6 mg/kg/day ÷ Q12 h Maximum 200 mg daily

Notes: Causes fatigue and exercise intolerance. Labetalol is both β- and α- blocker, so contraindicated in asthmatics and congestive heart failure due to negative inotropic effects. Use with caution in diabetics as it may mask hypoglycemia.

Ca++ Channel Blockers

CCBs	
Amlodipine (Norvasc, generic)	0.1–0.6 mg/kg/day ÷ Q12–24 h Maximum 10 mg daily
Felodipine (Plendil, generic)	2.5 mg/day given once daily Maximum 10 mg/day

Note: side effects include edema and gingival hyperplasia.

Central α-agonist

Central α-agonists	
Clonidine (Catapres)	10–30 μg/kg/day ÷ Q8–24 h Maximum 2400 μg/day
Clonidine transdermal patch (Catapres TTS)	TTS-1–TTS-III weekly

Note: causes significant fatigue.

Diuretics

Diuretics	
Spironolactone (Aldactone, generic)	1–3.3 mg/kg/day ÷ Q12 h Maximum 100 mg/day
Chlorothiazide (Diuril, generic)	10–20 mg/kg/day, given once daily Maximum 1000 mg/day
Furosemide (Lasix, generic)	0.5–6 mg/kg/dose ÷ Q12 h Maximum 600 mg/day
Hydrochlorothiazide (Hydrodiuril, Oretic, Microzide, Esidrex, generic)	1–3 mg/kg/day, given once daily Maximum 50 mg/day

Note: may cause dehydration, avoid in athletes.

Others

Peripheral α-antagonist	
Prazosin (Minipress)	5–100 μg/kg/dose ÷ Q8–12 h Maximum 500 μg/kg/day
Vasodilators	
Hydralazine (Apresoline, generic)	0.75–7.5 mg/kg/day ÷ Q6 h Maximum 200 mg/day
Minoxidil (Loniten, generic)	<12 years: 0.02–0.2 mg/kg/day ÷ Q12–24 h Maximum 50 mg/day >12 years: 10–40 mg/day ÷ Q12–24 h Maximum 100 mg/day

Note: Hydralazine may cause flushing, tachycardia, hypotension, and lupus-like syndrome.
Minoxidil causes hypertrichosis.

FOLLOW-UP

- After initiation drug therapy:
  - Every 2-4 weeks follow-up visit until BP control has been achieved.
  - Then q3-4 months thereafter.
  - Home BP monitoring and assessment for medication side-effects are important.
  - Periodic reassessment for hypertensive target-organ damage and laboratory monitoring should be performed.

What if ABPM is normal?

What if ABPM is normal?

- White coat hypertension

What if ABPM is normal?

- White coat hypertension
  - Is follow up needed?

Ambulatory BP/White Coat HTN

- In a group of 126 children, ABPM detected 58 subjects (46%) with white-coat HTN, 62 (49%)with stage 1 HTN and 6 (5%) with stage 2 HTN.
- In adults, white coat HTN may not be a benign condition (increased LVH and risks for sustained HTN).
- Limited data in children, but there may be a role in monitoring patients with white coat HTN.

Swartz, JS, et al. Pediatrics 2008; 122:1177.
Lande, et al. J Pediatrics 2008; 153: 50.
Flynn J. Curr Opin Nephrol Hypertension 2010; 19:292-297.

Prehypertension and White Coat HTN

- Recent debate calling for earlier intervention for HTN, especially those with prehypertension and WCH[1]
- Analysis of tracking studies confirms that high BP in the young predicts future high BP[2]
- Data showing reduced GFR and proteinuria in children with prehypertentions[3]

Collins RT, et al. J Pediatrics 2009; 155: 165-169.
Chen X et al. Circulation 2008; 117:3171-3180.
Lubrano R, et al. Ped Nephrol 2009; 24:823-831.

White coat hypertension

- Annual follow up with pediatric nephrologist or PCP recommended
- Reinforce lifestyle modification
- Relaxation techniques
- Annual ABPM may be of value in patients with WCH

Summary of HTN BPA

- Automatic alert for BP > 95% and reinforces follow up BP measurements
- If BP > 95% in children < 12 or > 130/80 in 13-17 years old on 3 occasions (3rd BP confirmed on auscultation), send pediatric nephrology referral/Dr. Advice
- If patient is symptomatic or history suggests acute pathology (glomerulonephritis, renal failure, end organ damage i.e. encephalopathy…), contact pediatric nephrology immediately

CASE 2

A 10 month old infant is seen in the ED with 3 day history of low grade fever, vomiting and diarrhea. The physical examination reveals a severely dehydrated infant. Wt 8.9 kg. Temp 101, HR 168/min, RR 33/min and BP 68/40. Patient's creatinine is 2.8.

What is your Dx and what should be further management?

Etiology of ARF

- Pre Renal
- Intrinsic Renal
- Post Renal

Work up

	Prerenal Failure	Renal Failure
U_{Na+} (mmol/L)	<20	>40
U_{Osm} (mOsm/L)	>500	<350 to 450
$U_{Cr} \div P_{Cr}$	>40	<20
$FE_{UricAcid} = U_{UricAcid} \div P_{UricAcid} : U_{Cr} \div P_{Cr}$	<12%	>20%
$FE_{Na+} = [U_{Na+} \div U_{Cr} : P_{Na+} \div P_{Cr}] \times 100$	<1%	>3%

$$FE\ Na = \frac{U\ Na}{P\ Na} \times \frac{P\ Cr}{U\ Cr} \times 100$$

ARF ETIOLOGY

PRE RENAL : DEHYDRATION, HEART FAILURE

POST RENAL : OBSTRUCTION

INTRINSIC RENAL : TUBULAR, GLOMERULAR VASCULAR, INTERSTITIAL

CLINICAL FEATURES OF ARF

1. Reduced Urine Output
2. Dehydration, Hypotension or Volume Overload, Hypertension, CHF
3. Uremia, Malaise, Nausea
4. Arrhythmia's with Hyperkalemia

Parameters to Monitor for Conservative ARF Management

- Strict I & O
- Daily, sometimes twice daily weights
- Q4 to 8H Serum Electrolytes, Cr/BUN Daily Serum Ca, Phosphate, Albumin
- May need to measure volume of urine or other drainage fluids for proper replacement
- ? of Central Venous Catheter for CVP

Prevention of ARF

1) Early Detection and Treating Cause
2) Fluid Challenge
   - 20 ml/kg Normal Saline
3) Furosemide or Mannitol

Management of ARF

1) Fluid Balance
2) Electrolyte Na, K, HCO_3
3) Nutrition
4) Use of Furosemide
5) Renal dose medication
6) Dialysis: Peritoneal or Hemo

Daily Fluid Management in ARF

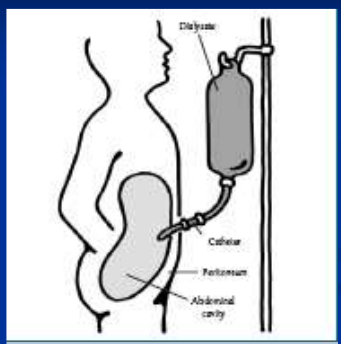
- For Insensible Losses : 30% of Normal Daily Fluid Intake or 400 ml/m^2/day
- Replace Urinary or Other Losses* :ml for ml

- Includes NG tube, other drains, diarrhea, vomiting, 3rd space fluids.
- Decrease for medication administration

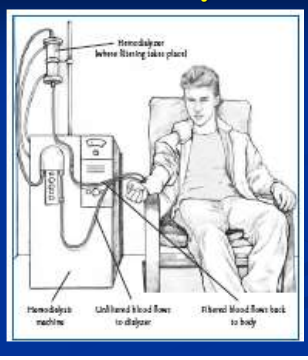
Renal Replacement Therapy in ARF

- Peritoneal Dialysis
- Hemodialysis
- CVVH, CVVHD
- Renal Transplantaion

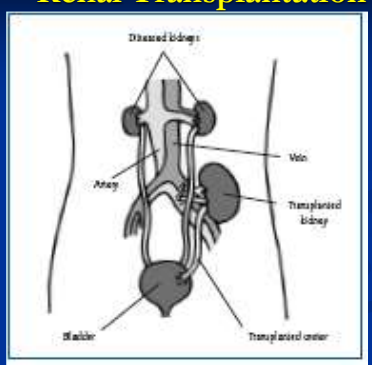
Peritoneal Dialysis



Hemodialysis



Renal Transplantation



Case 3

- Patient is a 8 year old male ex 25 weeker. He has been doing well since NICU discharge for prematurity, and was recently found to have elevated creatinine of 1.2 during a clinic visit to evaluate for short stature.

Case

- Does this patient have chronic kidney disease (CKD)?
- What defines CKD?
- How to determine his GFR?
- What complications need to be addressed?

CKD Staging

Stage	GFR (ml/min/1.73 m^2)
1	>90
2	60-89
3	30-59
4	15-30
5	<15 or dialysis

GLOMERULAR FILTRATION RATE

- **GFR** = volume of plasma ultrafiltrate presented to the nephrons per unit time in the process of urine formation.

GFR can be measured in 2 ways:

1. Directly measuring the **clearance** of an ideal filtration marker.
2. Using **equations** to estimate GFR.

ESTIMATING EQUATIONS

1. Cockcroft-Gault estimate
   - > 12 years old
2. Modification of Diet in Renal Disease (MDRD)
   - Adults with GFR < 60
3. Schwartz formula
   - Pediatric population

SCHWARTZ FORMULA

- GFR=(K *H)/S_{cr}
- GFR=ml/min/1.73m^2
- K=constant determined by Schwartz et al.
  K=0.413
- H=height in cm
- S_{cr}=serum creatinine in mg/deciliter.

Complications of CKD

- Anemia
- Blood pressure elevation
- Ca/phos: Renal Osteodystrophy
- Dialysis/transplant
- Electrolyte imbalance
- Fluid/nutrition
- Growth
- Hematological disorder
- Infection/immunization

Anemia

Causes

- Insufficient erythropoietin production
- Iron deficiency (poor nutritional intake)

Goal

- Hematocrit 33-36% and hemoglobin 11-12 g/dL for children with CKD
  - Epogen 30-300 units/kg/week (initial) and 60-600 units/kg/week (maintenance)
  - 2-3mg/kg/day of oral elemental iron
  - IV dextran/ferrlicit if iron saturation < 25%

Blood Pressure Elevation

- Renin-angiotensin system activation
  - ACEI (lisinopril, enalapril)
  - ARB (losartan)
- Fluid retention
  - Diuretics (furosemide, hydrochlorothiazide, spironolactone)
  - Salt restriction (< 2 gram/day, no added salt)

Ca/Phos: Renal Osteodystrophy

Ca/Phos: Renal Osteodystrophy

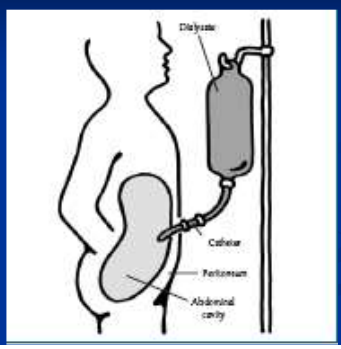
- Hypocalcemia
  - Decreased vitamin D 1,25 production
  - Complex with excess serum phosphorus
- Hyperphosphatemia
  - Decreased renal excretion
- Hyperparathyroidism
  - Caused by low serum calcium and vitamin D 1, 25
  - Weakens bone and cause fracture/deformity

Dialysis

Indications:

- Acidosis
- Electrolyte disorder
- Ingestion/intoxication
- Overload
- Uremia

Peritoneal Dialysis



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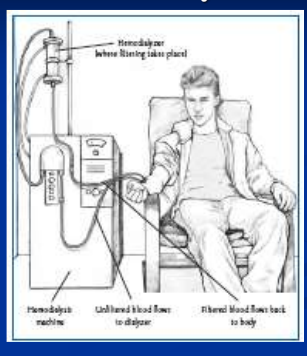
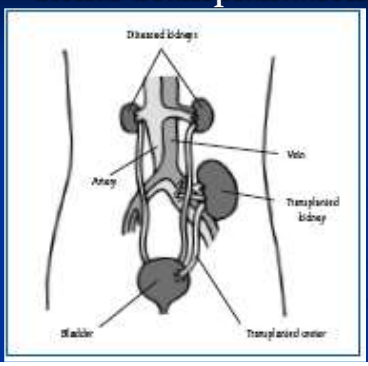


Renal Transplantation



Electrolyte Disorder

- Acidosis
  - Decreased renal bicarbonate reabsorption
  - Reduction of renal ammonia synthesis
  - Acidosis leads to protein degradation and efflux of calcium from bone
- Hyperkalemia
  - 90% of daily intake of potassium excretion occurs in the distal tubules
  - Less nephrons=less tubules=less potassium excretion=hyperkalemia

Fluid/Nutrition

- Low calcium, phosphorus, potassium
- Protein reduction 0.8-1.1g/kg/day in adults

Growth Failure

Causes

- Poor nutrition
- Anemia
- Acid-base imbalance
- Renal osteodystrophy
- GH and IGF-I resistance
  - Reduced GH receptors
  - Upregulations of GH inhibitors (i.e. SOCS)
  - Elevated IGF-binding proteins

Hematologic Disorder

- Hypercoagulable state in patients with SLE (anti-phospholipid syndrome) or nephrotic syndrome
- Renal patients are often on aspirin or coumadin therapy

Infection/Immunization

- All children with CKD should receive all routine immunizations including influenza and Prevnar
- Dialysis affects the immune system and can remove hepatitis B antibodies, so titers are measured periodically
- Live vaccines (Varicella and MMR) prior to renal transplant

Returning to our case

- Patient is a 8 year old male ex 25 weeker with multiple post-natal complications, including: "Anemia of prematurity status post Epogen treatment, Rickets of prematurity with three long bone fractures, Retinopathy of prematurity, and Chronic lung disease". He has been doing well since NICU discharge, and was recently found to have elevated creatinine of 1.2 during a clinic visit to evaluate for short stature.

Case

- Does this patient have chronic kidney disease (CKD)?
- What defines CKD?
- How to determine his GFR?
- What complications need to be addressed?

Case

Anemia: Hg = 14, Hct = 40.8, iron sat 40%
BP: 112/49
Ca/phos: Phos 4.9 Ca 10.3
  Vitamin D 25: 52 (normal)
  PTH 62 (normal)
Dialysis/transplant: NA
Electrolyte: K 4.8, CO_2 27
Fluid/nutrition: poor weight gain
Growth: <5% weight and height
  Maximize nutrition and start growth hormone therapy
Hematological disorder: NA
Infection/immunization: NA

QUESTIONS?

THANK YOU!