

The BP is up ... Now what?

Dan Feig, MD, PhD, MS

*Margaret M. Porter Professor of
Pediatrics*

Division of Nephrology

University of Alabama, Birmingham

February 8, 2020



**Children's
of Alabama**

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Disclosures

- **Consultant**
 - American Academy of Pediatrics
 - American Heart Association
 - Relypsa Pharmaceuticals (DSMB)
- **Council**
 - International Pediatric Hypertension Association (IPHA)
 - AAP-Society of Nephrology
- **ABP Nephrology Sub-Board**



Topics for Discussion

- Prevalence and impact of hypertension
- Common presentations of childhood hypertension
- Evaluation and management of hypertension
- Obesity related hypertension
- Hypertensive athletes
- ADHD and BP
- *Giraffes have higher blood pressure than any other animal*



320/200



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

The Scope of the Problem

- Affects >70 million Americans (29%)
- #1 risk factor for CV disease
- Major risk factor of stroke and ESRD
- Primary cause of 455,000 and contributes to 1,300,000/year
- Cost: >\$43 billion per year for meds
- Control Rates 52%
- Increased per capita expenditures associated with reduced control rates
 - Iriso et al. 2009 Int J Cardiol 137:124-131
- **Disease and its precursors develop in children**



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

13 yo boy with headaches

- Evaluation for frequent headaches
- No meds, no prior illnesses
- Wt: 85 kg, Ht 158 cm, BMI 34 kg/m²
- BP: 138/91



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Traditional Pediatric Approach to Hypertension



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Organ Injury at Diagnosis

- **CARDIAC**

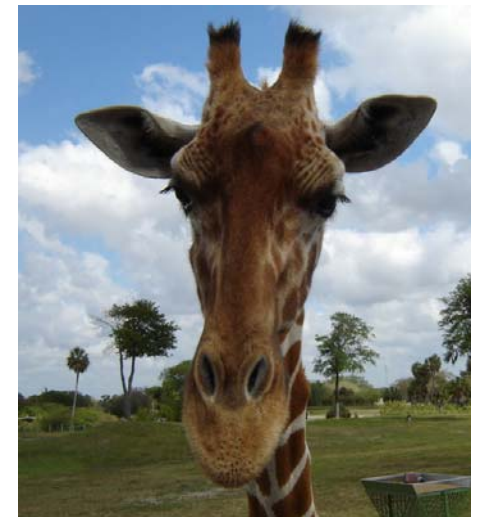
- Left ventricular hypertrophy
 - 42% LVMI criteria $>95^{\text{th}}$ percentile ($38\text{g}/\text{m}^{2.7}$)
 - 18% $>99.7^{\text{th}}$ percentile ($51\text{g}/\text{m}^{2.7}$)
 - Burke et al., Circulation 1987, 76:106

- **RENAL**

- Proteinuria
 - 26% have urine pro/Cr >0.3
 - 14% with essential htn, pro/Cr >0.3
 - Pontremoli et al., Am J Hypertens 1998, 11: 430

- **VASCULAR**

- Accelerated atherosclerosis (autopsy data)
 - Daniels et al., Circulation 1999, 82:1243



Neurocognitive Impairment in High Normal and Greater BP

- **Impaired Performance on Cognitive Tests (WISC, WRAT in NHANES III) Data**
 - 5077 kids: digit span, block design, math scores, down by 1 SD
 - Lande et al., Pediatrics 2003, 1143(6):720-724
- **Children with hypertension had impaired behavioral regulation, executive function and low transcranial Doppler-reactivity**
 - Ostrovskaya et al. J Child Neurol. 2015, 30:543-6



Symptoms of Hypertension

	Htn	Normal BP
Headache	42%	10%
Chest Pain	14%	4.9%
Abd Pain	10%	4%
Sleep Initiation	27%	6%
Tiredness	26%	6%
Concentration	10%	5%
School Failure	10%	3%



Croix and Feig, Ped Neph 2006, 21:527

So Why Measure BP?

- Hypertension causes target organ damage early in its course
- Hypertension adversely impacts neurocognitive development
- Hypertension negatively impacts quality of life
- Hypertension is a precursor to cardiovascular, cerebrovascular and renal disease



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Definition of Hypertension

AAP CPG for Management of Hypertension in Children and Adolescents (2017)

- Stratified by gender, age and height
- **Elevated BP:** 90-95% OR $>120/80$
- **Stage I Hypertension:** $>95%$ OR $>130/80$
- **Stage II Hypertension:** $>95%+12$ OR $>140/90$



On 3 Consecutive, encounters over $>2wks$



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Blood Pressure Tables

Systolic Blood Pressure- 11 year old Girl

	← Height Percentile →						
	5 th	10 th	25 th	50 th	75 th	90 th	95 th
<i>Ht (cm)</i>	135	138	142	147	152	157	160
50 th	98	99	101	102	104	105	106
90 th	111	112	113	114	116	118	120
95 th	115	116	117	118	120	123	124
95 th +12	127	128	129	130	132	135	136

Flynn et al. Pediatr 2017;140(3):e20171904



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Simplified BP Screening Table

Flynn et al. *Pediatr* 2017;
140(3):e20171904

Age, y	BP, mm Hg			
	Boys		Girls	
	Systolic	DBP	Systolic	DBP
1	98	52	98	54
2	100	55	101	58
3	101	58	102	60
4	102	60	103	62
5	103	63	104	64
6	105	66	105	67
7	106	68	106	68
8	107	69	107	69
9	107	70	108	71
10	108	72	109	72
11	110	74	111	74
12	113	75	114	75
≥13	120	80	120	80



**Children's
of Alabama**

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Evaluation of Hypertension: Initial Screening

- **Accurate measurement**
 - **Relaxed kid in exam room not vitals station**
 - **Callibrated Oscillometric Device**
 - **Appropriate Cuff**
 - **Length >80% arm circumference**
 - **Width >40% arm circumference at midpoint**
- **Confirm!!!**
 - **Measure on 3 different days**
 - **Consider ABPM**



13yo Overweight Boy

- **Recheck with large adult cuff: 119/62**
 - **>30% of referrals to Hypertension Clinic have either been checked only once or repeatedly with too small a cuff**
- **Weight loss, diet and exercise**
- **Annual BP checks at routine visits**



16 yo Overweight boy

- Evaluation for frequent headaches
- On methylphenidate 36mg daily for ADHD
- VS: Wt 88 Kg, Ht 167 cm, BMI 31.6kg/m²
- BP 139/89
- Stage 1 Hypertension >130/80
- Recheck with appropriate cuff in exam room:
136/88, 136/82, 133/84



Classes of Hypertension In Children

- **White Coat Hypertension**
 - 30-40% of referrals
- **Secondary Hypertension (20-30%)**
 - Renal (common) – **85%**
 - Cardiovascular (uncommon)
 - Drug use/abuse (uncommon)
 - Endocrine (very rare)
 - Tumor (very, very rare)
- **Essential Hypertension (70-80%)**



Evaluation of Hypertension: Stage 1 Hypertension

- Medical History
- Family History
- Physical Exam
- Urinalysis (including micro)
- Labs
 - Lytes, BUN, Cr
 - Lipid profile, glucose, drug screen
 - Endocrine Screening
- Imaging
 - Renal Ultrasound
 - Echocardiogram
 - ?EKG

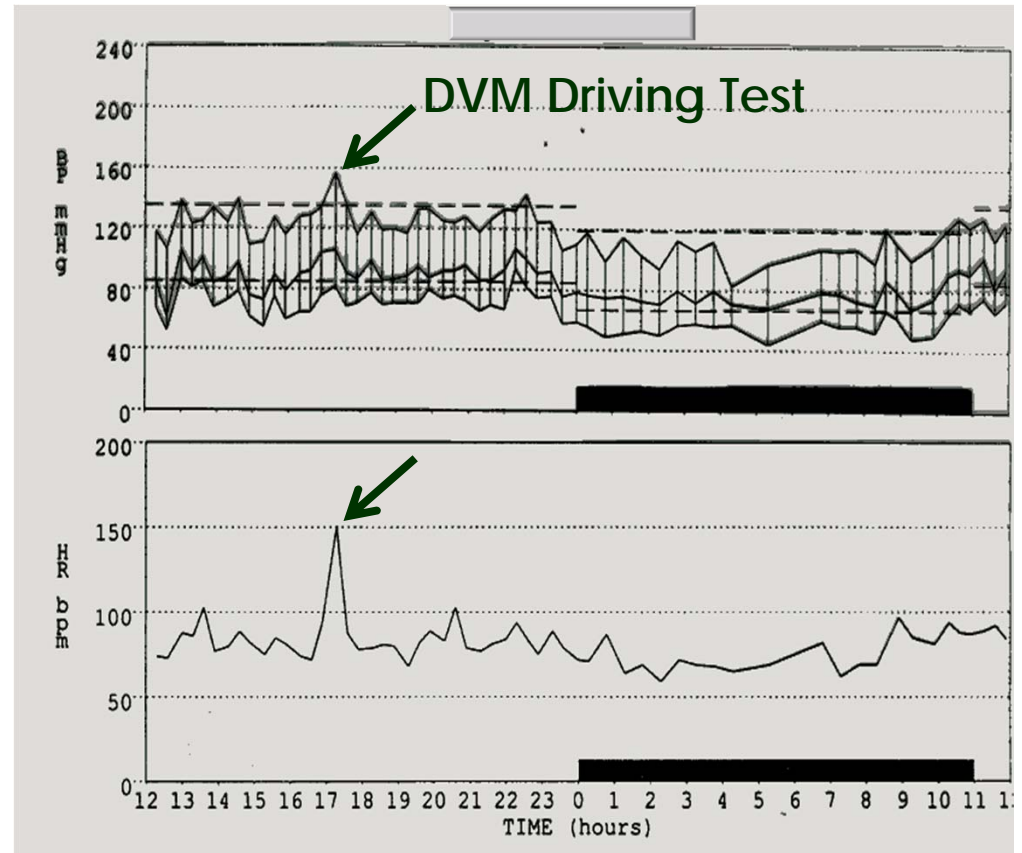
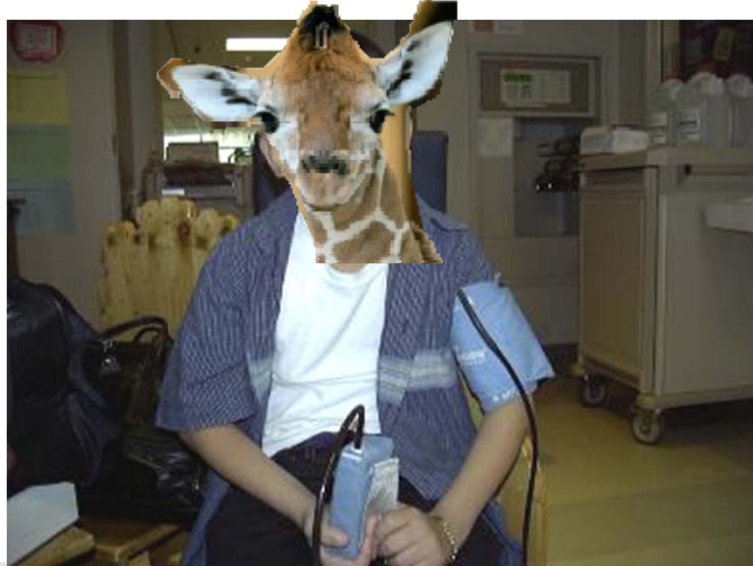


Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Ambulatory Blood Pressure Monitoring

- White Coat Hypertension
- Patterns
 - Mean & extremes
 - BP load
 - Chronobiology
 - **Nocturnal and TOD**



Dx: White Coat Hypertension



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Rx of White Coat Hypertension

- No medications
- Continue to measure BP at all contacts
- Screen and manage risk factors (i.e. obesity, inactivity, dietary indiscretions)
- *WCH is no protection against and is likely a risk factor for future hypertension*



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

ADHD and Childhood Hypertension Meta Analysis

- Assess BP Effects of Methylphenidate, Amphetamines, Atomoxetine
- 18 Studies, 3892 patients
- Statistically significant changes in SBP, DPB but small effect size
 - SBP mean +1.6mm,
 - DBP mean +1.7mm,
 - HR mean +3.7 bpm
- No change in prevalence of hypertension
- Magnitude same with stimulant and non-stimulant meds



Hennissen et al. CNS Drugs. 2017; 31:199

ADHD Meds - Outlier Effects

- BP means show little difference but frequency of outlier measurements increased in treated patients
- Among blinded RCTs, the prevalence of extreme outliers, BP $\Delta > 20$, or new stage 2 hypertension is 3.8-11x higher in treated vs placebo



Elia and Vetter. *Pediatr Drugs*. 2010; 12:165

Practical Summary: ADHD Meds and BP

- On a population level both stimulant and non-stimulant meds cause a statistically significant but minimal rise in SBP, DBP, HR
- Effects attenuate after 12mo
- Population studies suggest not a significant cause of hypertension
- 0.5-1% of treated subjects have large BP effects that are idiosyncratic and often resolve with a medication change



16yo Football Player

- 184cm, 132kg, BMI 39 kg/m²
- Casual BPs: 147/96, 145/95
- Confirmed hypertension by ABPM
- All labs and renal US normal
- Past Med history: obesity, no illnesses
- Family history: hypertension, early CVD



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

The Athletic Child



**Children's
of Alabama**

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Sudden Death in Young Athletes

• Hypertrophic Cardiomyopathy	36%
• Commotio Cordis	20%
• Congenital Coronary Anomalies	16%
• Cardiac Mass	7.5%
• Drug Abuse	5.3%
• Myocarditis	5.2%
• Valvular Disease	2.9%
• Aortic Rupture (Marfan)	2.1%
• Dilated cardiomyopathy	1.3%
• Asthma	2.1%
• Heat Stroke	1.6%



66% of events could have been predicted by echocardiography

Maron. NEJM 2003, 349:1064-1075



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Evaluation of Hypertensive Athletes

- **Confirm Hypertension**
- **Strongly consider ABPM**
- **Labs**
 - In ALL: CMP, UA
 - Consider: drug screen, others based on symptoms
- **Imaging**
 - Echocardiogram – soft recommendation
 - EKG NOT HELPFUL unless symptoms c/w arrhythmia



**Children's
of Alabama**

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Dietary Supplements

- **\$30 billion industry with celebrity testimonials and glitzy media**
- **Manufacturers need not demonstrate safety or efficacy before marketing**
- **Categories**
 - **Protein and calories supplements**
 - **Energy enhancers**
 - **Herbal and secret supplements**



**Children's
of Alabama**

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Hypertension and Sports Participation

Current Recommendations

- Stage 1 Htn: *Full Participation, monitor every 2 months until BP normal*
- Stage 2 Htn: *Restrict participation only until BP control is achieved, then monitor*
- Evidence of CV disease: *case by case*

*O'Connor et al., 36th Bethesda Conference: Curr Sports Med Rep. 2007
Apr;6(2):80-4*



Children's
of Alabama



UAB MEDICINE
PEDIATRIC NEPHROLOGY

Hypertension and Obesity



**Children's
of Alabama**

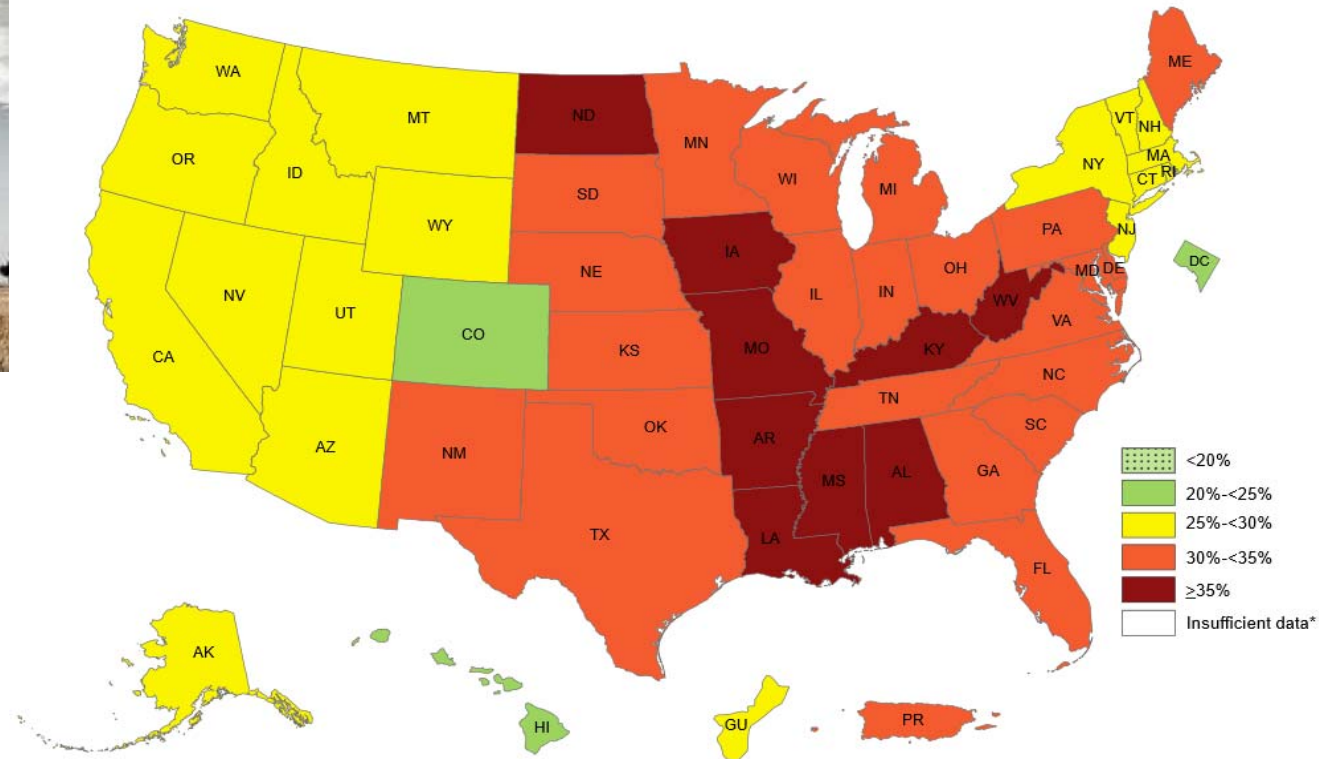
UAB MEDICINE
PEDIATRIC NEPHROLOGY

United States is "Well Rounded"

CDC State Obesity Rates, 2018



AL 36%



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Hypertension and Obesity

Obese children

- 18-32% have systolic hypertension
- 25-48% have pre-hypertension
- Acute weight gain/loss parallels BP



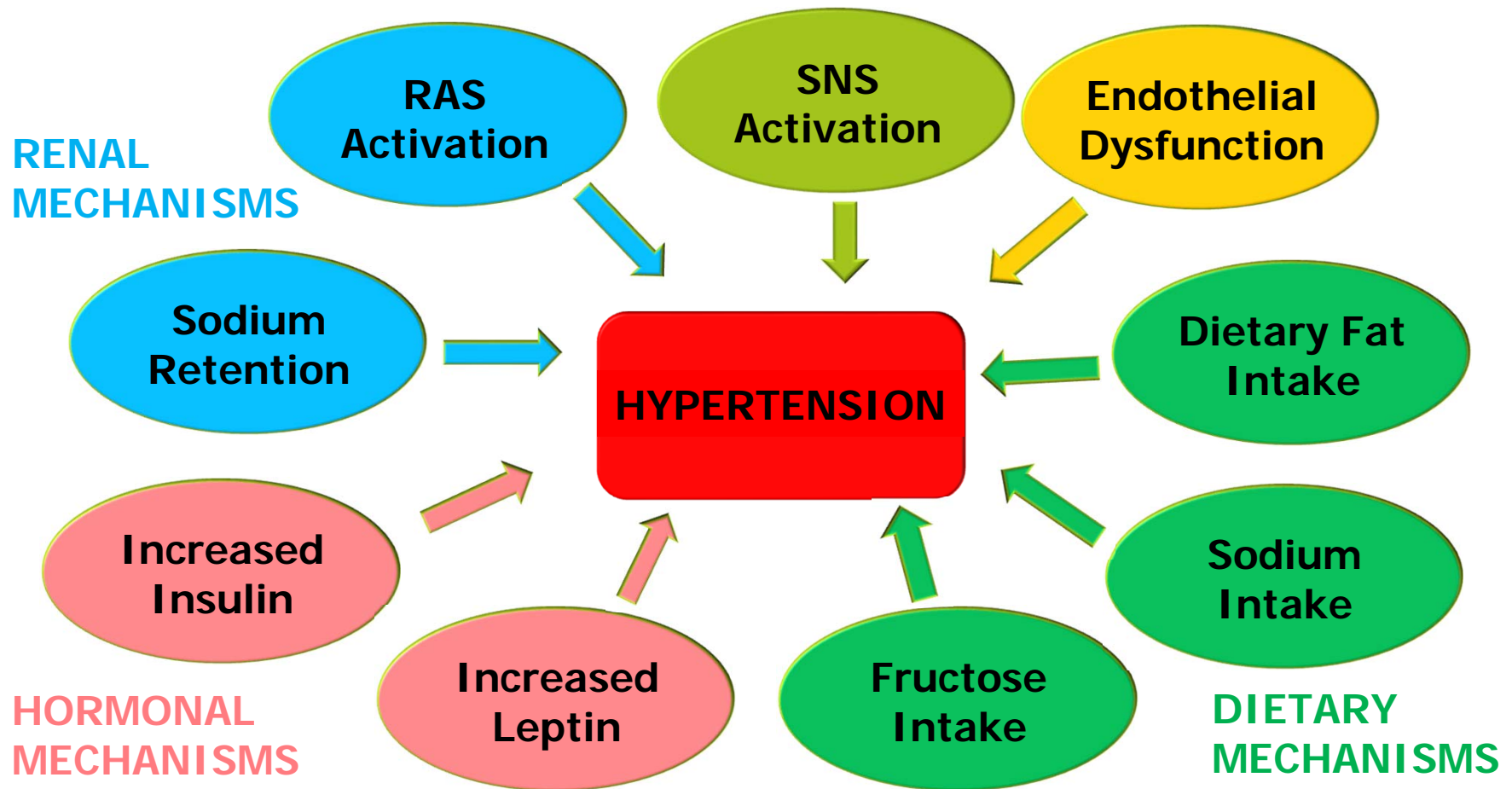
Approximately 72,000 children in Alabama have hypertension



Children's
of Alabama

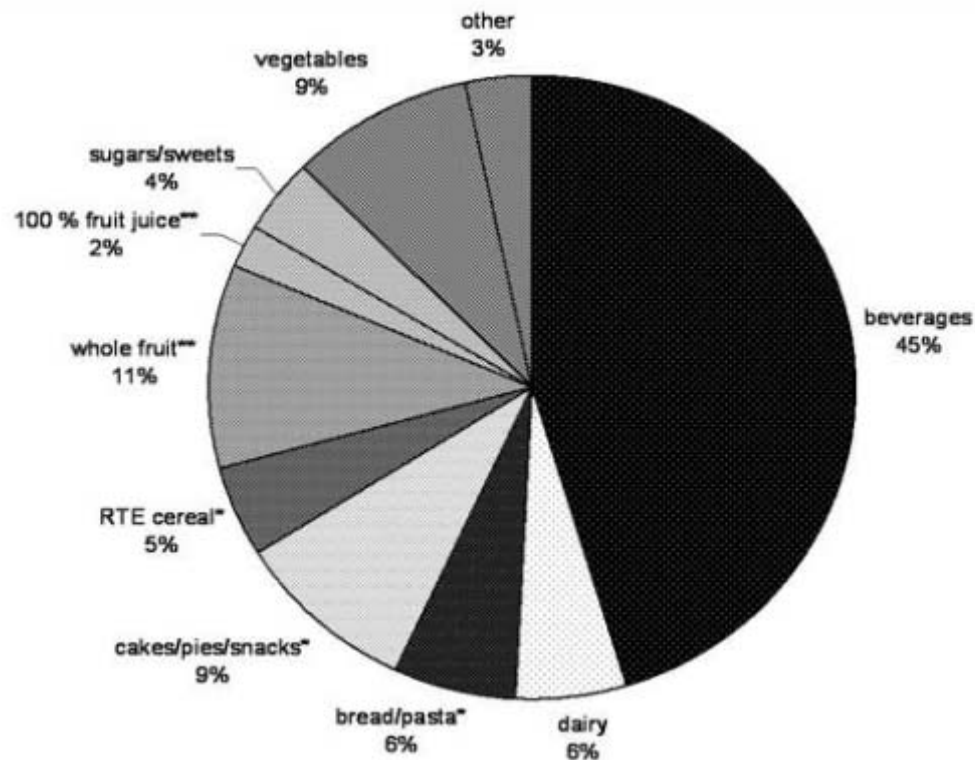
UAB MEDICINE
PEDIATRIC NEPHROLOGY

Mechanisms of Obesity Hypertension



Sugar Consumption in Adolescents

National Health and Nutrition Examination Survey (NHANES) 1988-1994



M. B. Vos, et al. Medscape Journal of Medicine. 2008; 10(7): 160.



**Children's
of Alabama**

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Health Risks of SSBs

- **Health Professionals F/U: top quartile of SSB intake had 20% increased risk of coronary disease, 34% increase risk of hypertension**
 - *De Koning et al. Circulation 2012; 123:1735.*
- **Each quartile of increasing SSB intake associated with 4mm Hg increase in DBP**
 - *Nguyen et al. J Peds. 2009, 154:807.*
- **Meta-analysis of data from 94 countries: each % point increase of caloric intake from sugar associated with 5% increase in T2DM risk**
 - *Siegel et al. Diabetes Res Clin Pract 2012; 96:76.*



It's the Quantity not the Source



Calorie and sugar counts of selected beverages

(Per 8-ounce serving; all juices are unsweetened)

Beverage	Calories	Grams of total sugar
Sprite	100	26
Pepsi	100	28
Coca-Cola classic	97	27
Gatorade G Cool Blue	50	14
Grape juice	152	36
Pineapple juice	132	25
Cranberry juice	116	31
Apple juice	114	24
Orange juice	112	21
Grapefruit juice	96	22



Sources: U.S. Department of Agriculture Nutrient Data Laboratory; company information
Graphics reporting by **KAREN KAPLAN**

Los Angeles Times



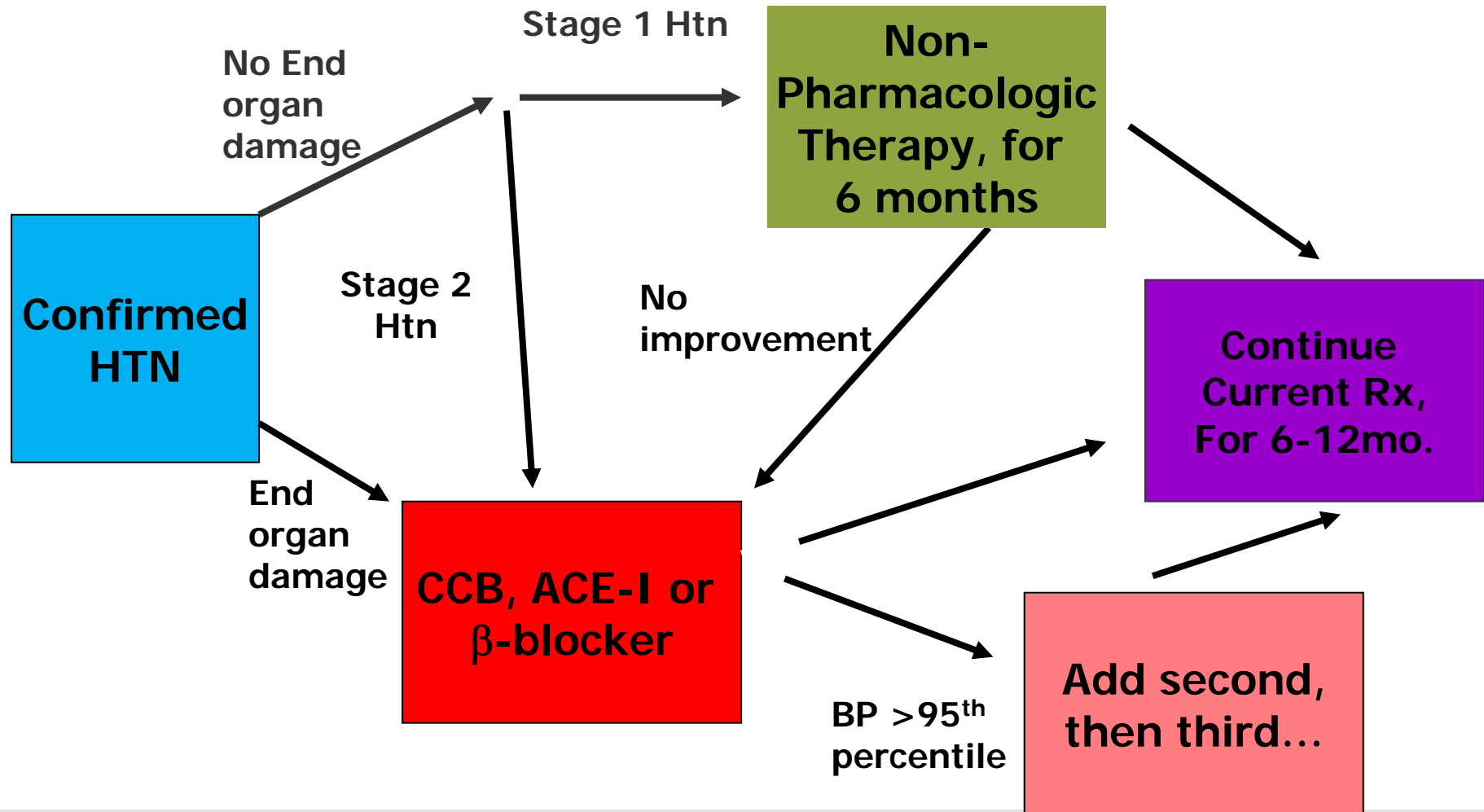
Gm sugar per
6oz serving



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Treatment Algorithm



Non-Pharm Therapy in HTN

Dietary Intervention

- Know where you are starting – Food Diaries
- Realistic calorie and content goals
 - <4gm Sodium per day
 - <100gm sugar per day
- Caffeine/Supplements – Beware the “Mt Dew Habit”
- Tobacco/Substance abuse
- **DASH for Kids** – Not magic, just proven
 - In clinical trials reduced BP 12/6

Exercise

- Structured/Supervised is best
- Must be at least 4 days per week
- Goal >45min per day



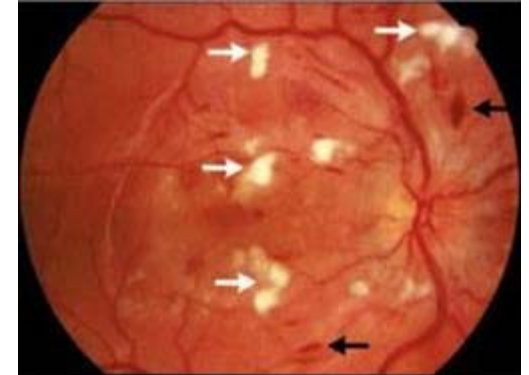
Medication Selection

- **Calcium Channel Blockers**
 - Essential or secondary hypertension
 - Poor for renin dominant hypertension
 - Less ideal in very obese
- **ACEi/ARBs**
 - Essential or secondary hypertension
 - Ideal for renin dominant hypertension
 - Important synergy with diuretics
 - High risk in pregnancy, dehydration
- **Beta Blockers**
 - Most often in patients with cardiac disease, CKD or anxiety disorder
 - Less optimal side effect profile especially in obese
- **Diuretics**
 - Often optimal second agent, especially fixed combination
 - First line in some obesity and steroid associated hypertension



15yo Female Swimmer

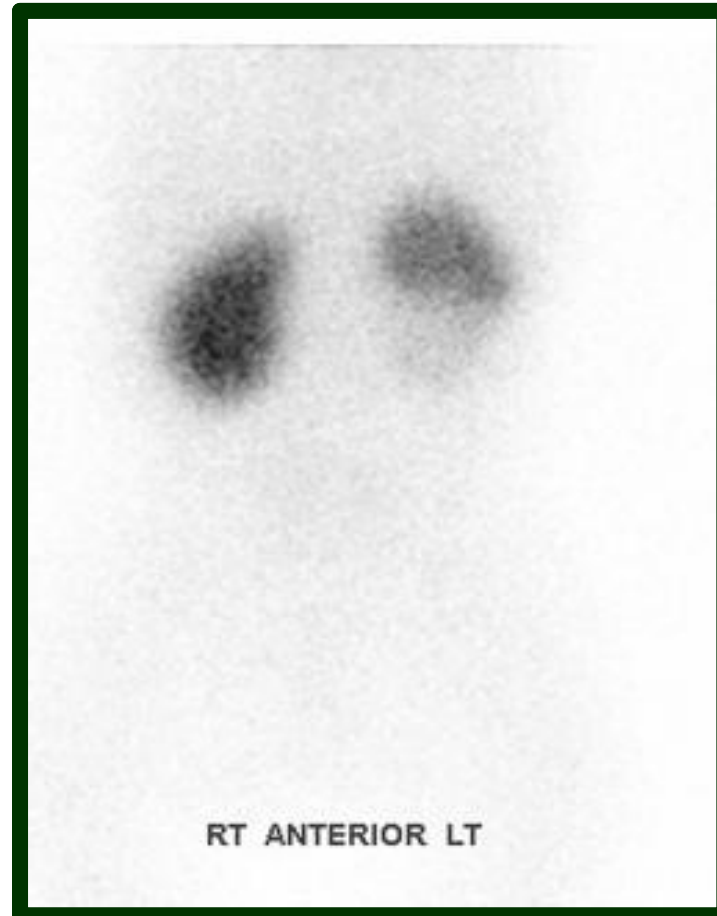
- Elite swimmer, told not to work out because of hypertension
- Medical history
 - BW 2300gm at 35 wks EGA, pre-eclampsia
 - Many ear infections, continued after PETs
- No meds, denies steroids, supplements
- BP 149/98 confirmed by ABPM
- BMI 22%, normal exam except retinas
- Na 141, K 3.1, Cl 102, HCO₃ 30, BUN 12, Cr 0.4
- Moderate LVH, proteinuria



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Renal Perfusion (DMSA)



**Children's
of Alabama**

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Renal Angiography (Different Child!!)

- RAS often not seen by renal US, in kids
- Renal asymmetry only with long ischemia
- Bruit only in 30%
- Non-invasive imaging is very sensitive



Renal or Renovascular Hypertension

- Stage 2 hypertension with cardiac target organ damage, \pm electrolyte abnormalities
- Medical therapy 1st ACEi/ARB
 - Monitor renal function, electrolytes
 - Caution with Mid-aortic and William Syndrome
- Angioplasty in renovascular htn often mitigates but doesn't cure and may need to be repeated
- Nephrectomy can be considered if refractory to medical therapy, often not curative



Hypertensive Crisis

- 17 yo boy comes to ER for headaches and decreased vision
- Father on HD for hypertension
- VS: HR 74, RR 22, **BP 198/114**
- Exam: confused, abdominal ascites, LE edema
- UA: +4 protein, trace blood,
- Labs: BUN 58, Cr 4.8, Ca 6.4,
- Head CT normal, Renal US small echogenic kidneys

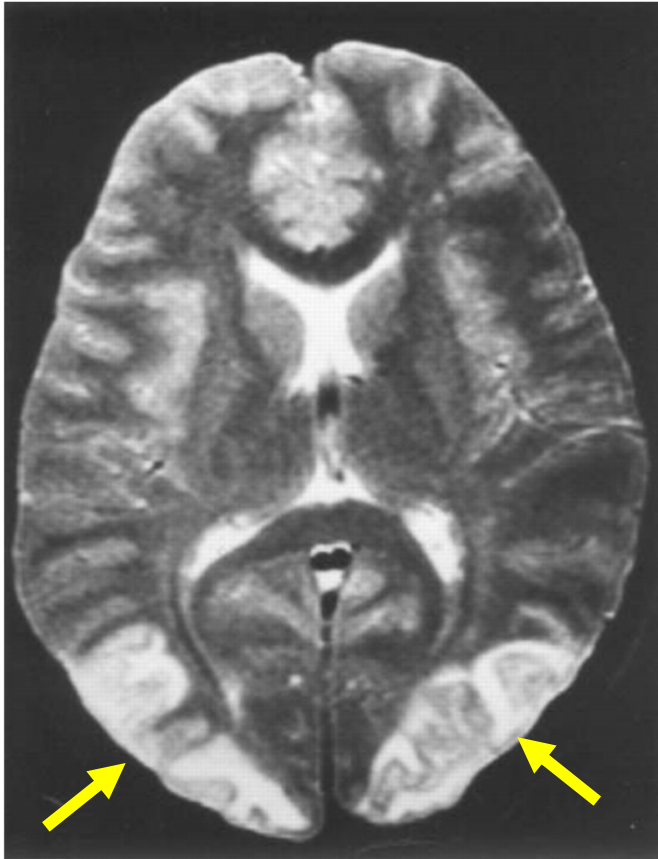


Evaluation of Hypertensive Emergencies

- **Confirmation of elevated BP**
 - Oscillometric measurement done correctly
 - Invasive arterial monitoring
- **Screening for secondary causes**
 - Medical and medication history
 - Physical Exam
 - Labs: Iytes, Cr, Hb, UA, UDS
 - Renal Ultrasound
 - Head CT or MR if CNS symptoms
- **Specialized Screening**
 - MRA or Angiography
 - Renal Biopsy



PRES: "Posterior" Reversible Encephalopathy Syndrome



(a)



Prasad et al. Br J Radiol 2007, 80:422



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Hypertensive Emergencies

Encephalopathy/Seizures
Cardiac Symptoms
Pulmonary Edema



IV Drips:

Labetolol 1-3 mg/kg/hr
Nicardipine 0.1-0.4 mg/kg/hr
Nitroprusside 1-8 mcg/kg/min
Esmolol 50-600 mcg/kg/min
Lasix 0.1-0.3mg/kg/hr

IV Bolus:

Hydralazine .15-.3 mg/kg

Oral, Rapid Onset:

Isradipine .05-.15mg/kg
Clonidine .05-.1 mg/kg

Long Acting:

CCB
ACE-I
 β -blocker



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Problems of Hypertension in Children

- Under-diagnosed/inadequate screening
- Significant target organ damage
- Significant reversible symptoms
- Developmental/intellectual impact
- Increasing prevalence
- Eventually becomes adult hypertension



Children's
of Alabama

UAB MEDICINE
PEDIATRIC NEPHROLOGY

Take Home Points

- **Accurate measurement**
 - Cuff size and confirmation
 - ABPM
- **Initial Evaluation to distinguish WCH/Essential/Secondary hypertension and diagnosis target organ damage**
- **Lifestyle modification is first line therapy for elevated BP and stage 1 essential hypertension**
- **ACEi, ARB and CCBs are usual first line, diuretics most common add-on therapy**
- **Most hypertensive athletes should continue to play**



The End



**Children's
of Alabama**

dfeig@peds.uab.edu

UAB MEDICINE
PEDIATRIC NEPHROLOGY