Hypertension in the well rounded child

ICD9 401.1 “benign” essential HTN

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San Antonio, Texas
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Disclosures

I disclose the following relationships with commercial companies:

Grant and Research Support from:
- Eli Lilly, Medtronic, Daiichi Sankyo, Parexel
- National Institute of Health

I do not intend to reference the investigational use of these drugs or products in my presentation today.

Learning Objectives

• At the end of this presentation, the participant will be able to:
  1. Recognize stage 1 & 2 hypertension in children and adolescents
  2. Treat primary hypertension in children using nonpharmacologic and drug therapy options
  3. Understand the risk for hypertension in children with type 2 diabetes

Hypertension in American children is common:
Hypertension is estimated to be prevalent in 4.5% of children

Underdiagnosis of hypertension:

• Analysis of the medical records of 507 hypertensive and prehypertensive children and adolescents over a span of seven years
• All the children visited an outpatient clinic at least three times
• 376 patients (74%) had undiagnosed hypertension
  80 patients (15.8%) had a true hypertension diagnosis
  7 patients had undiagnosed stage 2 hypertension
• Data to make the diagnosis of hypertension or prehypertension was present in the patients’ records

Adult Definition of Hypertension & “JNC 7” 2003 guidelines

• Adult 140/90 goals are based on evidence correlating BP data with adverse events
  - MI risk reduced by 20-25%
  - Stroke risk reduced by 34-40%
• 159/100= stage 1
• >160 = stage 2
The 4th Report on High Blood Pressure in Children and Adolescents

- BP standards based on sex, age, and height provide a precise classification of BP according to body size.

- The revised 2004 BP tables included the 5th - 99th BP percentiles; which allow for the staging of hypertension in children.

Example: Blood Pressure Levels for 12 year old Girls by Age and Height Percentile

<table>
<thead>
<tr>
<th>Age (Year)</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50th</td>
<td>101</td>
<td>60</td>
</tr>
<tr>
<td>90th</td>
<td>119</td>
<td>69</td>
</tr>
<tr>
<td>95th</td>
<td>127</td>
<td>77</td>
</tr>
<tr>
<td>99th</td>
<td>134</td>
<td>85</td>
</tr>
</tbody>
</table>

So Let’s Practice

- SAP is a 12 yo female in the 50th percentile of height and 95% for weight. Her manual BP on is 123/82 as she arrives for a visit.

- What is her BP percentile?

- What do we do with this information?
Blood Pressure 123/83 BP:
12 year old Girl with 50% Height Percentile

<table>
<thead>
<tr>
<th>Age (Year) Percentile</th>
<th>SBP (mmHg) Percentile of Height</th>
<th>DBP (mmHg) Percentile of Height</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 50th</td>
<td>101 102 104 106 108 109 110</td>
<td>59 60 61 62 63 64 65</td>
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<tr>
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<td>115 116 118 120 121 123 123</td>
<td>74 75 76 77 78 79</td>
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<td>99th</td>
<td>126 127 129 131 134 135</td>
<td>86 87 88 89 90 90 91</td>
</tr>
</tbody>
</table>

Stage 2 Hypertension
> 5 mm above 99%
Stage 1 Hypertension
95% to 5 mm above 99%
Pre-Hypertension
90-95% or >120/80

Normal
< 90%

Auscultation blood pressure measurement is gold standard

Manual auscultation blood pressure measurement is gold standard

- Cuff too small → high reading
- Cuff too big → usually not falsely low
- Prefer right arm if possible for comparison with BP normal values
- Repeat BP in both arms and one leg if elevated

Arm & Leg BP

A = B < C
BP can be 10-20 mmHg higher in the legs than the arms!

Korotkoff Sounds

- Artery collapses completely until the systolic pressure is greater than the cuff pressure with first audible sound of a thud or tap = SYSTOLIC
- Phase 2-4: systolic pressure opens the artery to produce increasing stage 2, 3 sounds then muffled blowing sound at phase 4.
- Silence at phase 5= diastolic BP reading
Oscillometric blood pressures
*measure mean arterial pressure and calculates SPB and DBP

Pediatric Symptoms of Hypertension
"silent disease"?
A recent study by Croix found that 51% of untreated hypertensive children when surveyed reported 1-4 Symptoms, and 14% reported more than four symptoms

3 most common symptoms
— headache
— difficulty initiating sleep
— daytime tiredness
These were all reduced with treatment

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
- 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
- Evidence of elevated intracranial pressure

Expert Panel On Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents
Pediatrics Dec 2011
NHLBI guidelines are designed for integration into the recommended pediatric health supervision visits in the AAP Bright Futures Guidelines

Integrated Cardiovascular Health Schedule
- Family History of Cardiovascular Disease
  - Obtain history by age 3 years
  - Men < 55 yo, Women < 65 yo with MI, stroke
  - dyslipidemia, HTN, DM, obesity, sedentary lifestyle
- Tobacco Exposure or Medications/Drug Use
- Nutrition/ Diet
  - Support breastfeeding optimal to 12 months
  - 2% milk at age 1-2 yr, fat free milk > 2 yr
  - Dietary guidance per growth curve

Integrated Cardiovascular Health Schedule
- Blood Pressure: Measure annually > 3 yo
- If < 90th % - repeat in 1 year
- If 90-95th % = prehypertension
  - Repeat by auscultation x 2 to confirm and repeat in 6 months
  - Diet, Activity, Weight management intervention
- If 95% to (99th% + 5 mmHg) = stage 1 HTN
  - Confirm on three occasions at least one week apart
  - Diet, Activity, Weight management *salt restriction
  - Review medications, examination and laboratory evaluation
- If > 99th% + 5 mmHg = stage 2 HTN
  - Refer to HTN expert within 1 week if possible and begin basic workup with dietary changes
  - Start anti-HTN medication
  - Follow q1-2 weeks until controlled
Clinical Evaluation of Confirmed Hypertension

<table>
<thead>
<tr>
<th>Study or Procedure</th>
<th>Purpose</th>
<th>Target Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>History, including sleep, history, family history, risk factors, diet, and habits such as smoking and drinking alcohol, physical examination</td>
<td>History and physical examination help focus subsequent evaluation</td>
<td>All children with persistent BP &gt;95th percentile</td>
</tr>
<tr>
<td>BUN, creatinine, electrolytes, urinalysis, urine culture</td>
<td>R/O renal disease and chronic pyelonephritis</td>
<td>All children with persistent BP &gt;95th percentile</td>
</tr>
<tr>
<td>CBC</td>
<td>R/O anemia, consistent with chronic renal disease</td>
<td>All children with persistent BP &gt;95th percentile</td>
</tr>
<tr>
<td>Renal ultrasound</td>
<td>R/O renal scar, congenital anomalies, or disparate renal size</td>
<td>All children with persistent BP &gt;95th percentile</td>
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</table>

Evaluation for Identifiable causes

Fasting lipid panel, fasting glucose To identify hyperlipidemia, identify metabolic abnormalities

Overweight patients with BP at 90th–94th percentiles; all patients with BP >95th percentile

Family history of hypertension or cardiovascular disease

Child with chronic renal disease

Drug screen To identify substances that might cause hypertension History suggestive of possible contribution by substances or drugs

Polysonmography To identify sleep disorder in association with hypertension History of loud, frequent snoring

“MONSTER”

- Medication (stimulants, OCP, NSAID, tricyclics, cocaine, ecstasy)
- Obesity
- Neonatal
- Symptoms
- Trends in Family
- Endocrine (hyperthyroid, pheochromocytoma)
- Renal

Common Causes of Hypertension by Age:

- **Infants**
  - Renal vein thrombosis, prior UAC
  - Renal artery stenosis
  - Congenital renal anomalies
  - Coarctation
  - BPD
  - Renal parenchymal disease
  - Renal artery stenosis
  - Coarctation of aorta
  - **82% is secondary HTN**

- **Children**
  - 1-6 year
  - 7-12 year
  - Renal parenchymal disease
  - Renovascular disease
  - Essential HTN
  - Renal parenchymal disease
  - Renovascular disease
  - **50% is essential HTN**

- **Adolescents**
  - Essential HTN
  - Renal parenchymal disease
  - Renovascular disease
  - **85-95% is essential HTN**

White Coat Hypertension

- A patient with BP levels above the 95th percentile in a physician’s office or clinic who is normotensive outside a clinical setting.

- Ambulatory Blood Pressure Monitoring: a newer technology which measures blood pressure every 15 minutes while awake and every 30 minutes while asleep (**Night time blood pressure should drop by 10%**)

Primary vs. secondary HTN?

Diagnosis for 246 patients aged 5–18 years with a mean age of 13.0±3.10 years from 4 pediatric nephrology centers:

- 15 (6%) secondary hypertension*
- 151 (61%) primary hypertension*
- 25 (10%) prehypertension, 8 (3%) white-coat hypertension
- 47 (20%) no hypertension

*There was no significant difference in the distribution of patients with stage 1 and 2 hypertension in the primary and secondary hypertension groups

Pediatrics Grand Rounds
12 April 2013

University of Texas Health Science Center
at San Antonio, Texas

Percentage of U.S. Children and Adolescents Classified as Obese, 1963–2008

The “Great” State of Texas:
- 2nd youngest population
- Highest number of children per family
- ~38% of US children
- ~20% of Hispanic children
- South Texas ~ 6.5 million people
- ~1.8 million children <18 years of age
- several of the fastest growing areas (Austin, San Antonio, McAllen, and Laredo)

Back to our San Antonio patient: she has now had repeat BPs on three occasions which were >95% and she has no laboratory or clinical evidence for an underlying etiology:

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Therapeutic Lifestyle Changes
- Family-based intervention improves success.
- Weight reduction = primary therapy for obesity-related prehypertension and hypertension.
- Physical activity* can improve efforts at weight management and may prevent future increase in BP.

*DASH: Dietary approaches to stop Hypertension
- Eliminate sugar containing drinks (soda, juice, sugared drinks)
- Decrease White Foods (pasta, rice, potatoes & SALT!)
- Increase Bright Color Foods (vegetables, fruits)
- Goal of < 2,300 mg salt for healthy people (one leveled teaspoon) and 1,500 mg for those with high blood pressure.

*Participation in sports — Children who have controlled high blood pressure are generally allowed to participate in competitive sports. Children and adolescents with high blood pressure are advised to avoid weight lifting until the blood pressure is better controlled. Exceptions to these recommendations include children with uncontrolled stage 2 hypertension, who are generally advised to avoid competitive sports.
Insulin Resistance and Puberty

Hyperinsulinism further increases reabsorption of Na and increases sympathetic tone.

Moran et al., J Clin Endocrinol Metab 2002; 87:4817-4820

Most Sodium Comes from Processed and Restaurant Foods

- Processed and restaurant foods: 73%
- Naturally occurring: 17%
- Added while eating: 5%
- Added in home cooking: 5%

What we’re up against

The contiguous United States, visualized by distance to the nearest McDonald’s

Intervention Effect Size Estimates of Behavioral Interventions on Systolic Blood Pressure

- BMI reduction of 10%: 5-15 mmHg
- Exercise intervention: 1-5 mmHg
- Salt restriction: 3-5 mmHg short term
- DASH type diet unknown but positive effect likely
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

Antihypertensive medications

Evidence based dosing and FDA approval for pediatric use is available in ALL these categories
- ACE-I: after age 2 preferred
- ARB: age 6 and older
- Diuretics
- Calcium Channel Blocker
- Beta Blockers
- Centrally acting alpha agonists
  - direct renin inhibitor, aldosterone antagonist not yet approved for children:

ACE Inhibitor:

- Avoid if suspecting renal artery stenosis
- Minimal rise in K, cough SE
- Discontinue ACE if markedly elevated hepatic serum enzymes develop or pregnant

Angiotensin Receptor Blockers

ARBs block Angiotensin II action
ex. irbesartan, losartan – age 6 and older

Angiotensin Receptor Blocker interferes with the binding of angiotensin II to angiotensin I receptors
- do not use in pregnancy or marked liver elevation
Calcium channel blockers

Block the entry of calcium into the cells which decreases vascular peripheral resistance

*Ex: amlodipine- long half life*

Other agents

- **Beta Blockers**: propranolol – avoid in DM, asthma, athletes
- **Centrally acting alpha agonists**: clonidine
  - Not yet approved for children: direct renin inhibitor, aldosterone antagonist

Step-wise Approach to Therapy

1. Start with a small dose of an ACE, ARB or CCB anti-hypertensive drug with once daily monotherapy preferred
2. Increase initial anti-hypertensive drug until BP <95%: expect 5-10 mm HG change for each dosage increase
3. Add a small dose of a second drug (often diuretic) once monotherapy at maximal dose
4. Increase dose of second anti-hypertensive medication until BP <95%*

Target-Organ Abnormalities in Children with Hypertension

- Target-organ abnormalities are detectable in hypertensive children and adolescents.
- LVH is the most prominent evidence of target-organ damage and can be evaluated with echocardiography
- The presence of LVH is an indication to initiate or intensify antihypertensive therapy
Important Adult BP Trials with Pediatric Implications

• ALLHAT
  – All drug classes equally effective in BP treatment and CVD mortality reduction
  – 64% of adults required 2 drugs for BP control
  – Some classes had better outcomes in secondary analyses (diuretics, ACE inhibitors usually)
• Trophy
  – Treating pre-hypertension (ARB) prevents the onset of future hypertension

Sad but True

80% of Diabetic patients will either die from or have a major cardiovascular event

One of my first patients that I treated at UTHSCSA for Type 2 Diabetes lost 140 lbs before he died of a heart attack at age 23 at UHS

Primary Aim:
Comparison of three treatment regimens on time to failure (loss of glycemic control) in children and adolescents with Type 2 Diabetes

Multiple secondary Outcomes
Included:
  • Cardiovascular disease risk
  • Microvascular & Macrovascular complications

TODAY Study Group. NEJM, 2012

Major Comorbidities at Baseline and New (New = <4 years average time in study)

<table>
<thead>
<tr>
<th>Met alone</th>
<th>Met + rosi</th>
<th>Met + lifestyle</th>
</tr>
</thead>
</table>
| Hypertension
  baseline | 12% | 12% | 11% |
  new | 25% | 23% | 19% |
| Dyslipidemia – LDL
  baseline | 4% | 3% | 3% |
  new | 8% | 7% | 6% |
| Dyslipidemia – Trig
  baseline | 22% | 16% | 16% |
  new | 9% | 12% | 9% |
| Microalbuminuria
  baseline | 9% | 3% | 6% |
  new | 11% | 12% | 9% |

TODAY Study Group, NEJM, 2012
In Summary

- Hypertension in American children is a growing epidemic
- High blood pressure is estimated to be prevalent in 4.5% of children and up to 75% of cases may be missed in clinical care
- Hypertensive obese children have metabolic factors increasing their risk for early cardiovascular disease which is accelerated by hyperinsulinemia and/or T2Diabetes

The way to keep your health is to eat what you don't want, drink what you don't like, and do what you'd rather not.  

Mark Twain

References

  <http://www.abenews.go.com/Health/CardiacHealth/>.

Echocardiography Measures by Treatment Group (median and quartiles)

- LA diameter indexed by height (population median 2.0 cm/m)
- LV mass indexed by height$^{1.75}$ (population median 30 g/m$^2$)

References

ACE inhibitors

- Renal side effects: Patients with renal artery stenosis should not receive ACE inhibitors because they maintain glomerular filtration by efferent arteriolar vasoconstriction, which is blocked by ACE.
- Metabolic side effects: moderate, often clinically insignificant rise in potassium due to a mild reduction in serum aldosterone concentrations and beneficial effect on plasma insulin levels
- Hepatic side effects: a rare syndrome that begins with cholestatic jaundice and progresses to fulminant hepatic necrosis and (sometimes) death. Discontinue ACE if markedly elevated hepatic serum enzymes develop
- Racial Differences: African American children do not respond to ACE inhibitor therapy as well as children of other races
- Pregnancy: major congenital malformations after first-trimester exposure to ACE inhibitors. It is not known whether this may apply to all other classes of drugs that block the renin–angiotensin system

BP tables for Infants

Suppose his actual SBP is 120 mmHg (BP), his SBP 2-score is then: SBP 2-score = (x − μ)/σ = (120–109.46)/10.7128 = 0.884
The corresponding SBP percentile = 0.960 is 95% > 90%. This indicates that the child is normal.