Kennsla læknanema á 5. námsári

Hypertension in Children

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Introduction

- Hypertension is the number one risk factor for death throughout the world.
- Suboptimal BP (>115 mm Hg SBP) is responsible for approximately 60% of cerebrovascular disease and 50% of ischemic heart disease.
- Hypertension is both an important cause and consequence of chronic kidney disease.

The *World health statistics 2012 report*

F. M. Tedla et al, Int J Hypertens, 2011

Introduction

- In the Muscatine study *(Lauer, Pediatrics 1989)*
  - Children with systolic pre-hypertension were 4 times more likely to be hypertensive as adults.
  - Children with diastolic pre-hypertension were 2 time more likely to have hypertension in adult life.
- The Bogalusa Heart Study *(Bao, Am J Hypertens 1995)*
  - Prevalence of hypertension in young adults was much higher in subjects whose childhood BP was in the top quintile.

Childhood blood pressure “tracks” into childhood

- Hypertensive young adults may, therefore, have had long-standing hypertension with its attendant risk of vascular damage and premature cardiovascular events.

Definition of hypertension in children

How do we defince childhood hypertension?

- Complications of long-standing hypertension are rare in children and the serious hypertensive target-organ damage, commonly seen in adults, can not be used to guide the diagnosis and treatment of pediatric hypertension.
- The US National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents.
- Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents, 2017.

Pediatrics. 2017;140(3):e20171904

How do we defince childhood hypertension?

- The report provides age, gender and height specific blood pressure reference values which are now widely used for the diagnosis of childhood hypertension, both in the clinic and scientific research.
- The reference values (blood pressure percentiles) are based on the normative distribution of 50,000 single BP measurements in healthy **normal weight** children.
  - *Pediatrics. 2017;140(3):e20171904*

Í fullorðnum tekur skilgreining á háþrýstingi hins vegar mið af hættu á marklíffæraskemmdum, sem er lítil í börnum.

Viðmiðunargildi taka mið af aldri, kyni og hæð

TABLE 3. BP Levels for Boys by Age and Height Percentile

Age, y	BP Percentile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82

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Definition of hypertension

Guidelines published by the Working Group

Viðmiðunargildi taka mið af aldri, kyni og hæð, flokkun verður þó einfaldari frá og með 13 ára aldri.

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

*Blood pressure percentiles are age, gender and height specific.

Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Pediatrics. 2017;140(3):e20171904

TABLE 2. Recommended Dimensions for BP Cuff Bladders

Age Range	Width, cm	Length, cm	Maximum Arm Circumference, cm*
Newborn	4	8	10
Infant	6	12	15
Child	9	18	22
Small adult	10	24	26
Adult	13	30	34
Large adult	16	38	44
Thigh	20	42	52

* Calculated so that the largest arm would still allow the bladder to encircle arm by at least 80%.

Indications for 24°ambulatory blood pressure monitoring

- Confirm diagnosis of hypertension
- White coat hypertension?
- Confirm nocturnal dip
- Diagnose masked hypertension
- Study therapy response
- Annual assessment of high risk children, such as transplanted children

Epidemiology of childhood hypertension

Table 1 Prevalence of hypertension in children and adolescents from screening studies

Study location	Number screened	Age (years)	Number of screenings	Normative criteria	Prevalence	Reference
Edmonton, Canada	15,594	15–20	1	150/95	2.2 %	Silverberg et al. [14]
New York, United States	3,537	14–19	2	140/90	1.2 % SHTN 2.4 % DHTN	Kilcoyne et al. [15]
Dallas, United States	10,641	14	3	95th percentile	1.2 % SHTN 0.4 % DHTN	Fixler et al. [16]
Minneapolis, United States	14,686	10–15	1	1987 TF	4.2 %	Sinaiko et al. [17]
Tulsa, United States	5,537	14–19	1	1987 TF	6.0 %	O'Quin et al. [18]
Minneapolis, United States	14,686	10–15	2	1996 WG	0.8 % SHTN 0.4 % DHTN	Adrogue et al. [19]
Houston, United States	5,102	12–16	3	1996 WG	4.5 %	Sorof et al. [20]
Houston, United States	6,790	11–17	3	4th Report	3.2 % HTN 15.7 % PHTN	McNiece et al. [21]
Reykjavík, Iceland	1,071	9–10	3	4th Report	3.1 %	Steinthorsdottir et al. [22]
Changsha, China	88,974	12–17	3	4th Report	3.1 % HTN 7.2 % PHTN	Cao et al. [23]

DHTN diastolic hypertension, *PHTN* pre-hypertension, *SHTN* systolic hypertension, *TF* Second Task Force Report [24], *WG* Working Group Report [25], *4th Report* The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents [13]

Author and year of publication:
Silverberg, 1975
Siniako, 1992
Adrogue, 2001
Sorof, 2004
McNiece, 2007
Steinthorsdottir, 2011
Cao, 2012

Flynn J. Pediatr Nephrol. 2013, 28:1059-66

Prevalence of hypertension in 9- to 10-year-old Icelandic children

- Cross-sectional study of 970 healthy school children.
- 3 blood pressure screening sessions.

Steinthorsdottir S. J Clin Hypertens 2011;13:774-9

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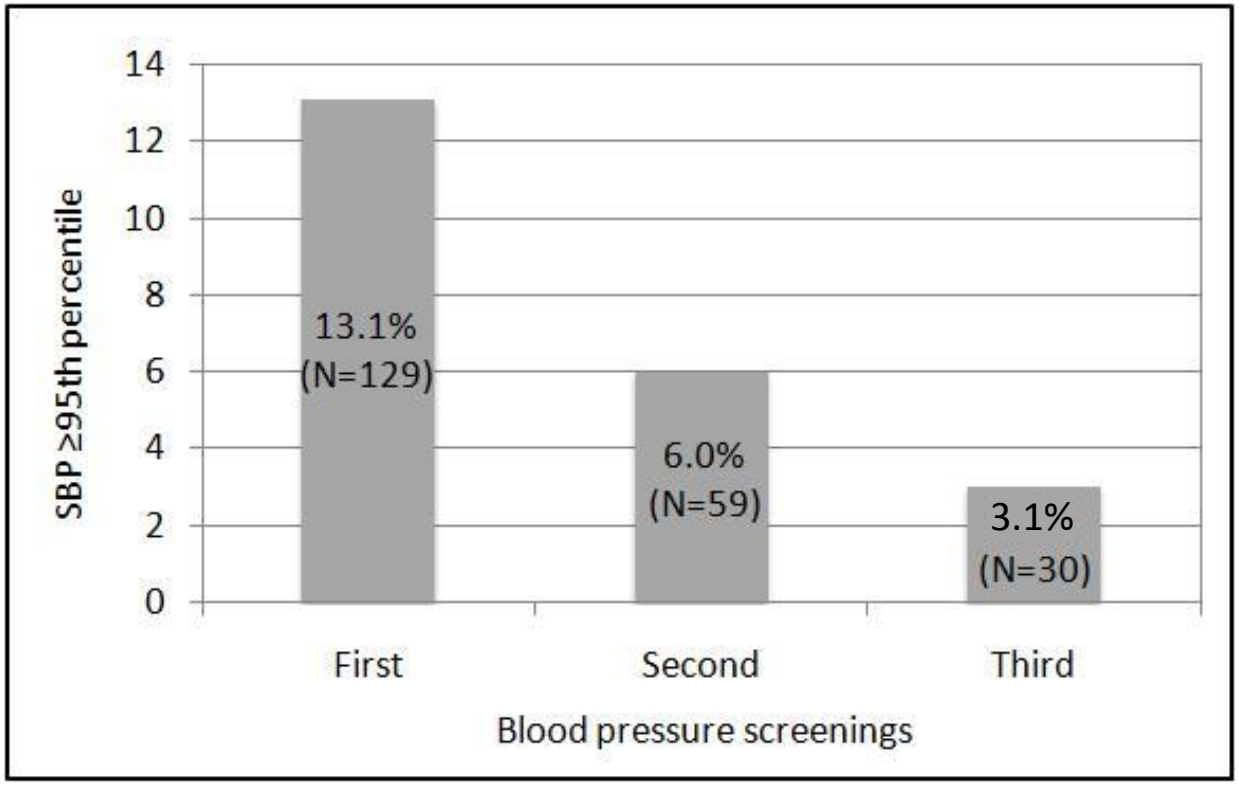
Prevalence of hypertension in 9- to 10-year-old Icelandic children



Íslensk rannsókn

Sustained HTN, 2.5%
White-coat HTN, 0.6%

- Cross-sectional study of 970 healthy school children.
- 3 blood pressure screening sessions.

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Steinthorsdottir S et al. J Clin Hypertens 2011

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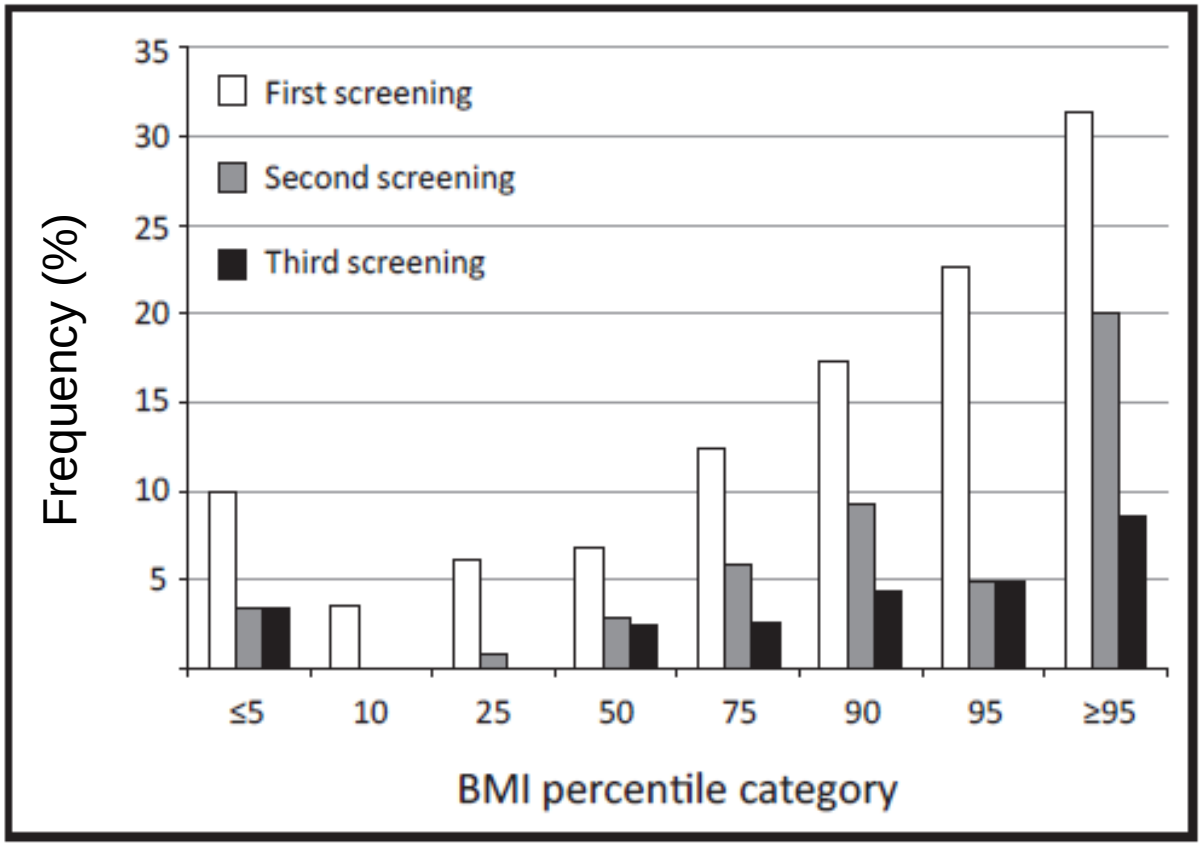
Íslensk rannsókn



Effect of BMI percentile on frequency of elevated blood pressure at the first, second and third screening sessions.

Steinthorsdottir S. J Clin Hypertens 2011;13:774-9

Prevalence in US children and adolescents

- A study by Sorof et al carried out in Houston Texas *(Pediatrics 2004)*
  - The prevalence of HTN in young adolescence
    - was 4.5% in 5102 children age 13.5 ± 1.7 years
    - 2% in the lean children (BMI ≤5th percentile)
    - 11% in the obese children (BMI ≥95th percentile)

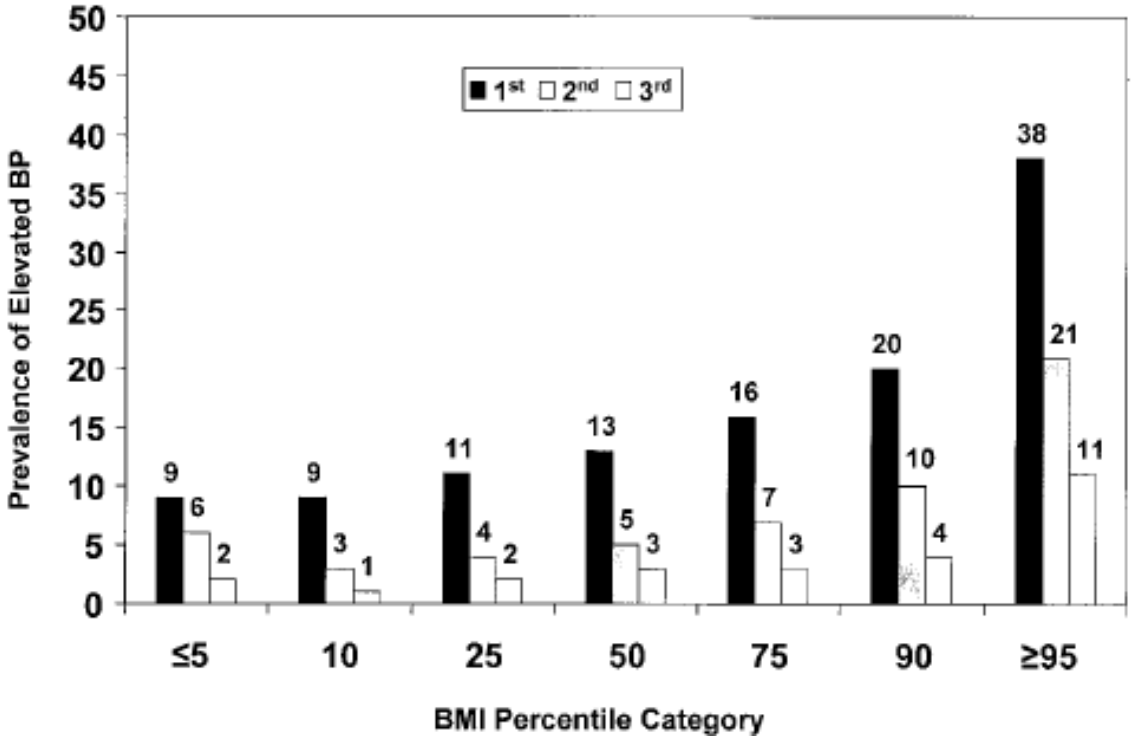


Fig 3. Prevalence of elevated blood pressure at first, second, and third screening categorized by BMI percentile. The numbers on top of each column represent prevalence of elevated blood pressure for that category.

Aetiology of hypertension in children and adolescents

Aetiology of Childhood Hypertension

	Infants	**School-age**	**Adolescents**
Primary/Essential	<1%	15-30%	85-95%
Secondary	99%	70-85%	5-15%
Renal Parenchymal Disease	20%	60-70%	
Renovascular	25%	5-10%	
Endocrine	1%	3-5%	
Aortic Coarctation	35%	10-20%	
Reflux Nephropathy	0%	5-10%	
Neoplastic	4%	1-5%	
Miscellaneous	20%	1-5%	

Flynn JT. Hypertension in childhood and adolescence. In: Kaplan NM, Kaplan's Clinical Hypertension, 9th ed. Philadelphia, PA: Lippincott-Williams and Wilkins, 2005, pp. 465-488.

Obesity has significantly affected the prevalence of childhood primary hypertension

- The worldwide childhood obesity epidemic has had a profound impact on the frequency of hypertension and other obesity-related conditions.
- Primary hypertension should now be viewed as one of the most common health conditions in the young.

Yfirþyngd og offita eru nú stærsta ástæða háþrýstings hjá börnum og unglingum

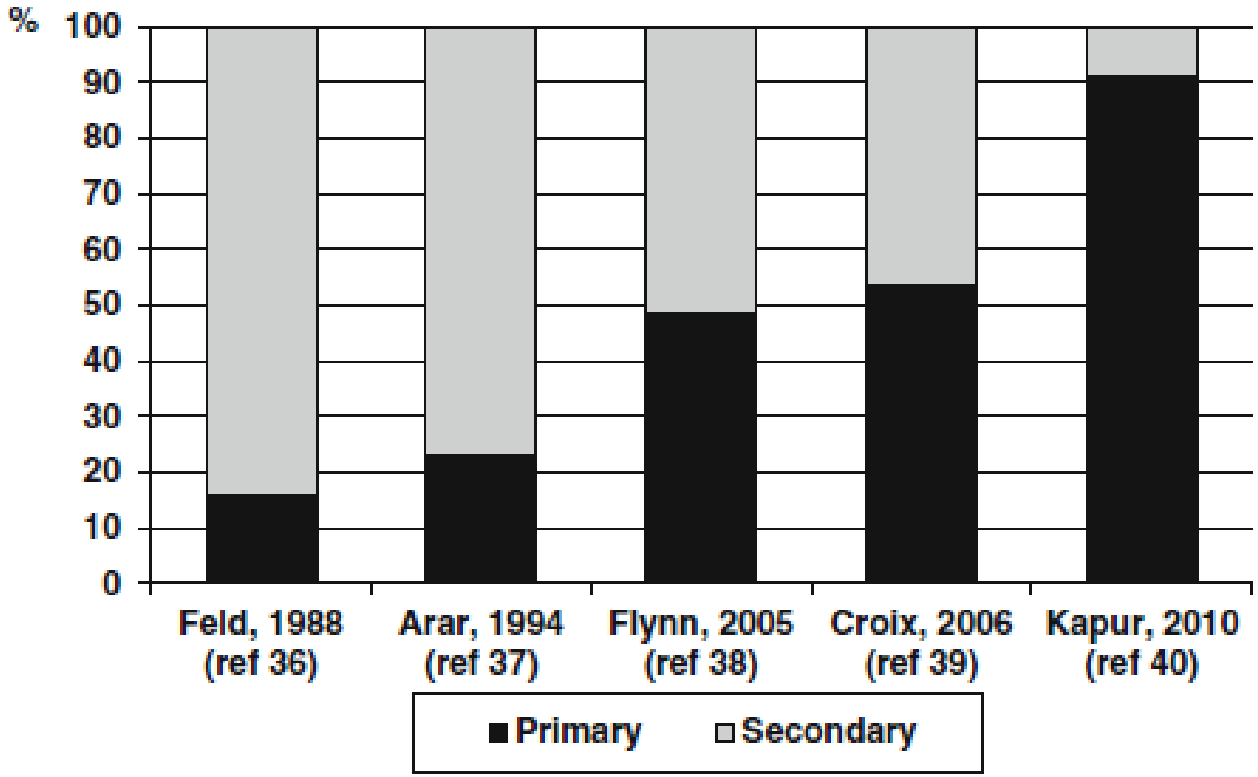


Fig. 1 Frequency of primary hypertension in pediatric referral series

Flynn J., Pediatr Nephrol. 2013, 28:1059-66

Hypertensive target-organ damage in children

Left ventricular hypertrophy and future cardiovascular events

- LVH is an independent predictor of cardiovascular events in adults
  - *(Koren, Ann Intern Med 1991; Brown, Am Heart J 2000; Levy, N Engl. Med 1990).*
- Although outcome-based standards for LVMI are not available in children
  - Left Ventricular Hypertrophy
    - has been used as a marker to identify hypertensive children at risk for future cardiovascular events.
      - *(Brown, Am Heart J 2000; Levy, N Engl. Med 1990)*
    - should be an indication for aggressive antihypertensive therapy.
      - *(The Fourth Report on the Diagnosis, Evalulation and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics 2004)*

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Prevalence of LVH in children and adolescents with HTN

- Essential hypertension
  - 46% - Daniels SR, 1998 Circulation
  - 41% - Hanevold C, 2004 Pediatrics
  - 40% - Litwin M et al; 2006 Pediatr Nephrol
  - 24% - Flynn JT, 2005 Pediatr Nephrol
- Secondary hypertension
  - Similar as in essential hypertension
    - Hanevold C, 2004 Pediatrics

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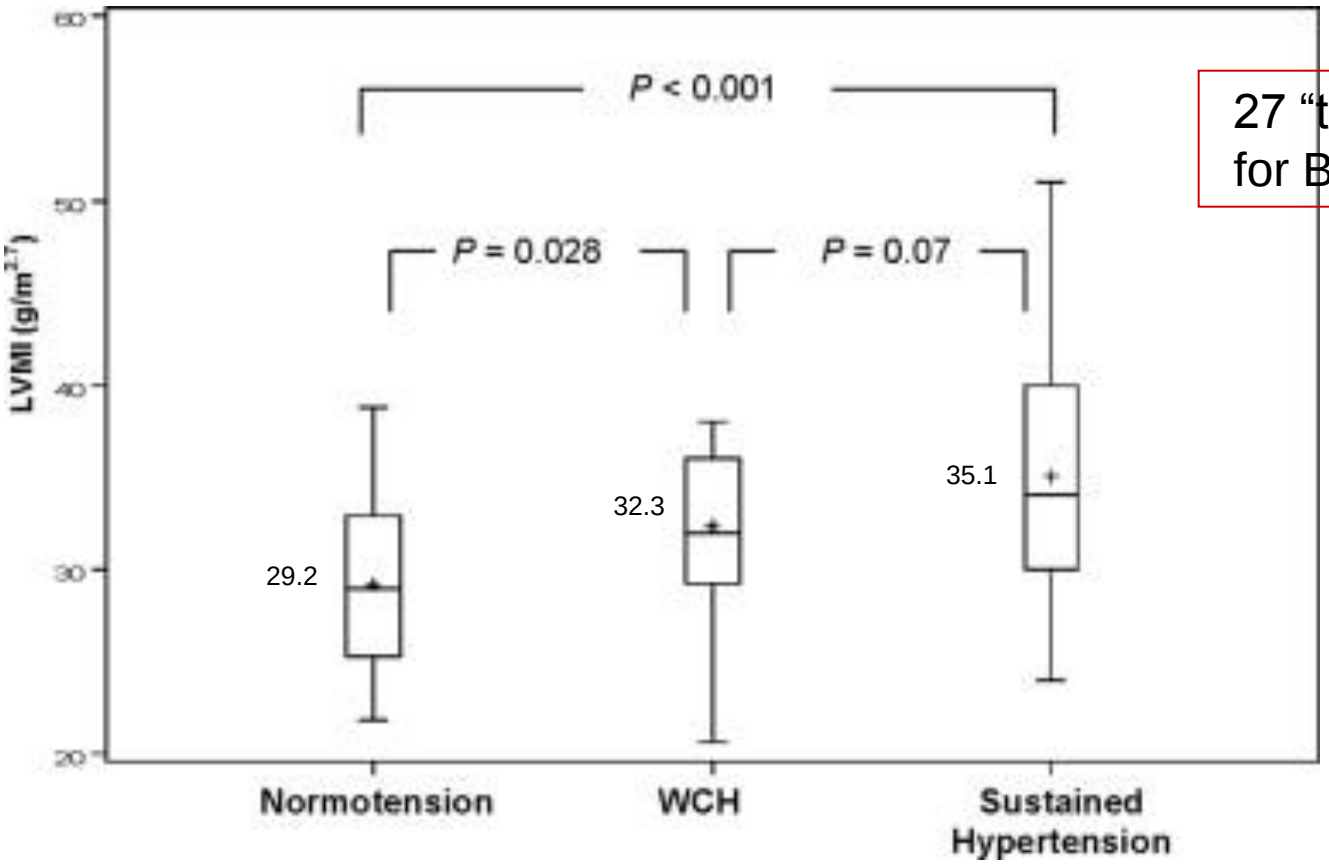
Left Ventricular Mass Index in Children with White Coat Hypertension



27 “triplets” matched for BMI and gender

Lande M. J Pediatr 2008;153:50-4

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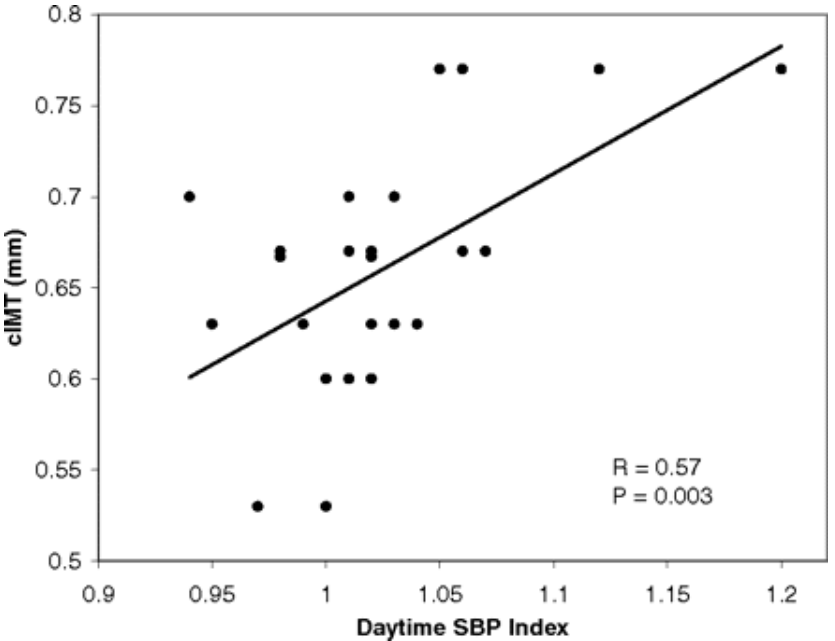
Effects of childhood primary HTN on carotid intima media thickness (cIMT): a matched controlled study

- 28 hypertensive children underwent an evaluation of their cIMT.
- When controlled for BMI
  - cIMT correlated strongly with daytime systolic blood pressure index in hypertensive subjects.
  - and the median cIMT was greater in hypertensives than matched controls (0.67 versus 0.63 mm; *P*=0.045).
  - these results provide strong evidence that cIMT is increased in childhood primary hypertension, independent of the effects of obesity.

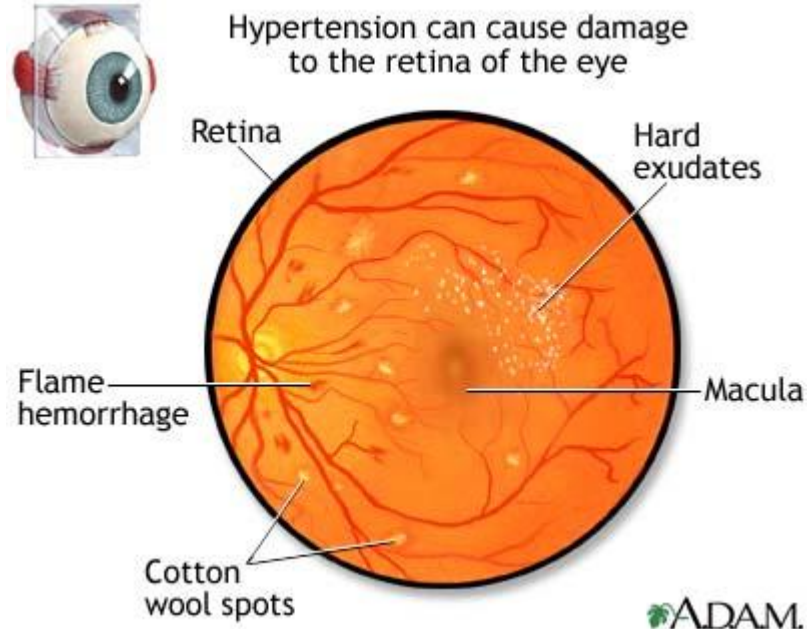
Lande, Hypertension 2006



Hypertensive retinopathy

Í raun mjög sjaldgæft fyrirbæri hjá börnum og unglingum

- Few studies of retinal abnormalities have been conducted in hypertensive children.
- High childhood blood pressure (SBP) has, however, been associated with retinal arteriolar narrowing *(population based study of 1572 children; Mitchell, Hypertension 2007).*
- Daniels et al *(Am J Ophthalmol 1991)* described evidence of mild retinopathy in 50 (51%) of 97 children and adolescents with essential hypertension.



Microalbuminuria

- Microalbuminuria is associated with CVD in hypertensive adult patients
  - *Jager, Arterioscler Thromb Vasc Biol 1999*
- Limited literature on micro-albuminuria in non-diabetic children with hypertension.

Childhood blood pressure and vascular damage in adult life

Pediatr Nephrol (2010) 25:323–328
DOI 10.1007/s00467-009-1350-3

ORIGINAL ARTICLE

Háþrýstingur á barnsaldri spáir fyrir um marklíffæraskemmdir hjá fullorðnum – íslensk rannsókn

Blood pressure in children and target-organ damage later in life

Asthildur Erlingsdottir · Olafur S. Indridason · Olafur Thorvaldsson · Vidar O. Edvardsson

- Study of the association between childhood BP and TOD in adult life.
- 126 cases, 54 male and 72 female.
- Elective admission for minor surgical procedures to Landspitali University Hospital in Reykjavik, between 1950 and 1967.
  - Median age at childhood admission, 15 (10-18) years.
  - Median age at follow-up 58 (42-68) years.
- A significant correlation was found between the diagnosis of **coronary artery disease** at follow-up and childhood systolic BP (odds ratio = 1.052; P = 0.03) and elevated BP (BP≥95th percentile) (P = 0.03).

The Cardiovascular Risk in Young Finns Study

- A population based, prospective cohort study
  - Over 2200 adult Finns aged 24-39 years first examined at the ages of 3-18 years.
- Carotid intima-media thickness, a marker of vascular damage, at the age of 33-39 years was significantly associated with
  - Hypertension and other cardiovascular risk factors assessed at the age of 12 years.

Raitakari, JAMA 2006

Evaluation of children with hypertension

Lykilatriði: uppvinnslan miðar að því að skoða þetta tvennt.

- The evaluation should
  - Distinguish between primary and secondary causes of hypertension.
  - Look for hypertensive target-organ damage.

Treatment of childhood hypertension

Life style modifications

- Weight reduction should be attempted in all overweight hypertensive patients.
- Regular excercise.
- Dietary modification.

Indications for initiation of pharmacotherapy and BP goal

Ábendingar fyrir lyfjameðferð

Clinical indication	Blood pressure goal
Persistent hypertension despite therapeutic lifestyle modification	<95th percentile
Hypertension with associated end-organ damage	<90th percentile
Hypertension in the setting of chronic kidney disease	<90th percentile
Hypertension in the setting of diabetes mellitus (types 1 or 2)	<90th percentile
Secondary hypertension	<90th percentile
Symptomatic primary hypertension	<95th percentile

Current European Society of Hypertensions treatment goals:

- Uncomplicated hypertension, BP% <90%
- CKD, BP <75%
- CKD + proteinuria, BP <50%

Ferguson M. Pediatr Nephrol, 2013

Targeted pharmacotherapy of hypertension

Sömu lyf og hjá fullorðnum

Table 3 Indications for targeted drug therapy

Condition	Drug
Renovascular hypertension	ACE–I, ARB, diuretic, vasodilator
Coarctation of aorta	Beta-agonist
Chronic kidney disease	ACE-I, ARB
Obesity-related hypertension	ACE-I, ARB
Hypertensive athlete	ACE-I, ARB, CCB

ACE-I angiotensin-converting enzyme inhibitor; *ARB* angiotensin II receptor blocker; *CCB* calcium channel blocker; *GC* glucocorticoid

Ferguson M. Pediatr Nephrol, 2013

Summary

- Childhood blood pressure tracks into adulthood and young adults may, therefore, have long-standing hypertension and increased cardiovascular risk.
- The recent upward trend in prevalence of pediatric hypertension, related to the obesity epidemic, is indicative of a significant emerging public health problem.
- Target organ damage is common in children and adolescents with sustained hypertension.
- Timely diagnosis and treatment of hypertension in children and adolescents is important to prevent future organ damage.