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**Hacettepe University
Ankara**

Hypertension: Etiology, Diagnosis, ABPM and Management

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Outline

- Definition of hypertension (HTN) in children
2016, ESH Guideline
- Etiology
- Evaluation
 - Medical history, physical examination
 - Investigations
 - Target organ damage
- ABPM, home BP measurement
- Management of HTN

Definition of HTN in children

- Adults:
 - Based on CV morbidity and mortality
- Children:
 - Arbitrary, based on the normal distribution of BP in healthy children
 - Not based on CV morbidity and mortality
- Hypertension is defined as average **SBP and/or DBP** that is
 - **≥ 95th percentile**
 - **for age, gender, and height**
 - **on three or more occasions**



Consensus Document

2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents

Empar Lurbe^{a,b}, Enrico Agabiti-Rosei^c, J. Kennedy Cruickshank^d, Anna Dominiczak^e, Serap Erdine^f, Asle Hirth^g, Cecilia Invitti^h, Mieczyslaw Litwinⁱ, Giuseppe Mancia^j, Denes Pall^k, Wolfgang Rascher^l, Josep Redon^{b,m,n}, Franz Schaefer^o, Tomas Seeman^p, Manish Sinha^q, Stella Stabouli^r, Nicholas J. Webb^s, Elke Wühl^t, and Alberto Zanchetti^u

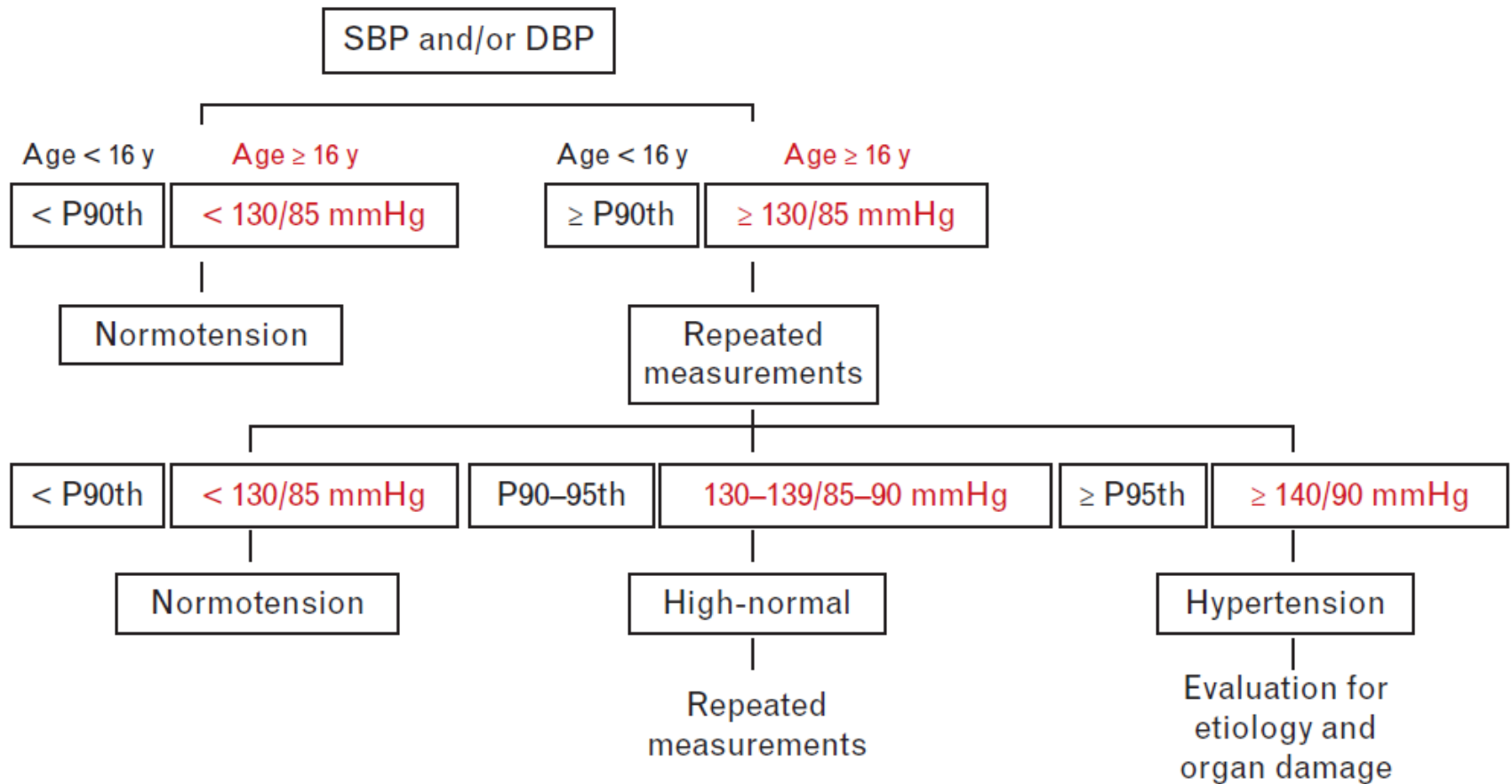
15	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

15	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

Modified from Task Force on High Blood Pressure in Children and Adolescents [7]. Boxed area corresponds to reference values of boys 16 years or older in which the reference values for adults are recommended. BP, blood pressure.

Classification of HTN in children and adolescents

	0–15 years SBP and/or DBP <u>percentile</u>	16 years and older SBP and/or DBP <u>values (mm Hg)</u>
Normal	<90th	<130/85
High-normal	90th to <95th percentile	130-139/85-89
Hypertension	≥95th percentile	≥ 140/90
Stage I hypertension	95th percentile to the 99th percentile and 5 mm Hg	140-159/90-99
Stage II hypertension	>99th percentile and 5 mm Hg	160-179/100-109
ISH	SBP ≥95th percentile <u>and</u> DBP <90th percentile	≥140/<90



2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents

..... Because of the **persisting lack of European reference values that incorporate age, sex and height, throughout the entire pediatric age range, we confirm the decision of the 2009 ESH Guidelines to use the normative data on auscultatory clinic measurements provided by the US Task Force**, providing BP percentiles for each sex, ages from 1 to 17 years and for seven height percentile categories.

Prevalence

• Switzerland ¹	2.2%
• Hungary ²	2.5%
• Poland ³	4.9%
• Overweight or obese (Germany, Austria, Switzerland) ⁴	22.0%
• Turkey ⁵	
– Normal BMI	5.5%
– Overweight	7.6%
– Obese	11.4%

1. Chiolero A, et al. J Hypertens 2007; 25: 2209–2217.
2. Katona E, et al. Blood Press 2011; 20: 134–139.
3. Ostrowska-Nawarycz L, et al. Kardiol Pol 2007; 65: 1079–1087.
4. Sorof JM, et al. Pediatrics 2004; 113: 475–482.
5. Duzova A, et al. NDT 2013; 28 (Suppl. 4): iv166–iv171.

Obesity and hypertension

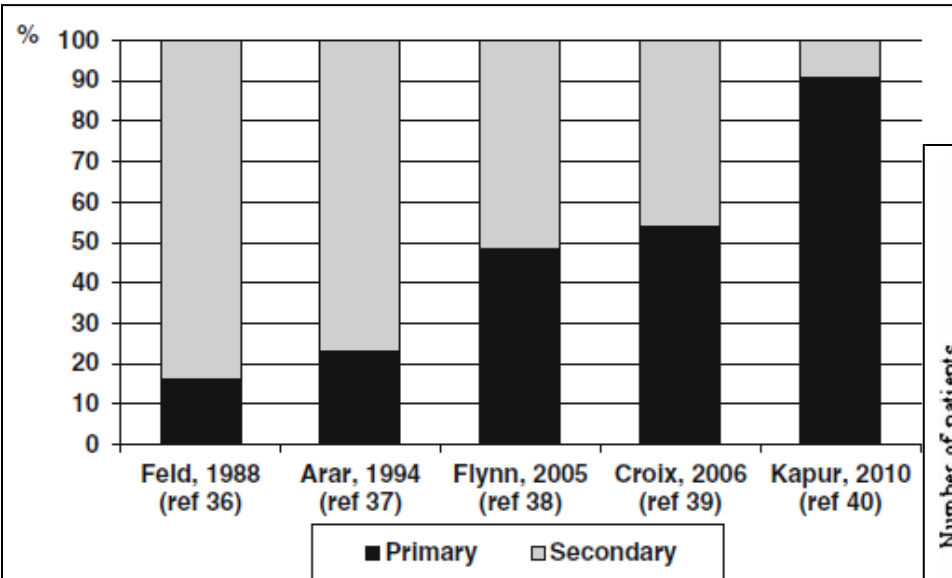


Fig. 1 Frequency of primary hypertension in pediatric referral series

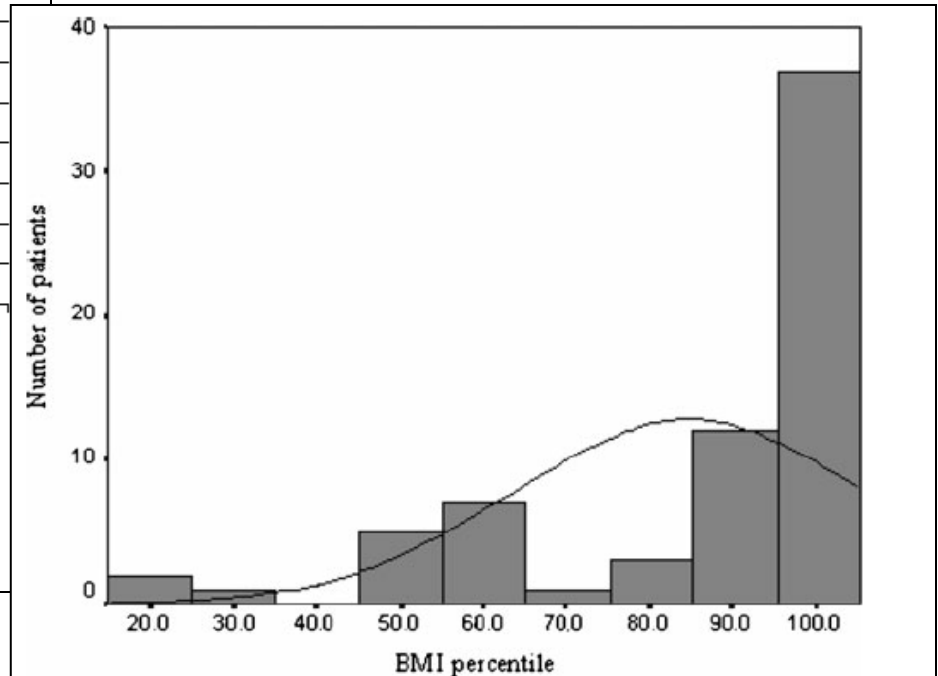


Fig. 2 Distribution of body mass index (BMI) percentiles among 70 children with primary hypertension

Incidence

- Adolescents; 10-19 years¹
 - Normotension → HTN 0.4/100 patients/year
 - High-normal → HTN 1.1/100 patients/year
- Masked HTN → Sustained HTN² 7/100 patients/year
- Type 2 diabetes³ 4/100 patients/year
- Obese (compared to normal)⁴
 - 2 fold increase
 - Severe obesity: > 4 fold increase
- Repair of coarctation of aorta⁵ 1.3/100 patients/year

1. Redwine KM, et al. J Pediatr 2012; 160:98–103.
2. Lurbe E, et al. Hypertension 2013; 62:410–414.
3. TODAY Study Group. Diabetes Care 2013; 36:1735–1741.
4. Parker ED, et al. Pediatrics 2016; 137:1–9.
5. Bocelli A, et al. Pediatr Cardiol 2013; 34:620–629.

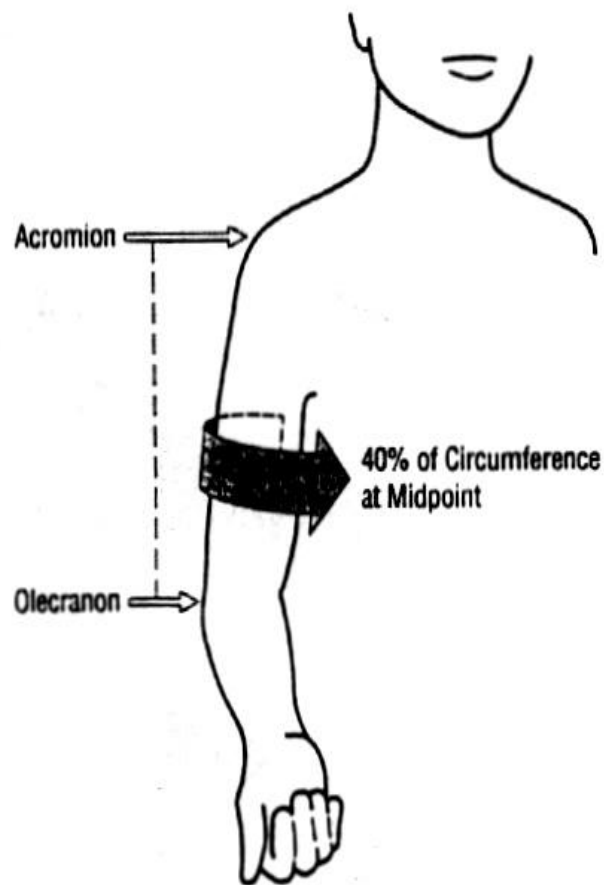


Fig 2. Determination of proper cuff size: step 1. The cuff bladder width should be approximately 40% of the circumference of the arm measured at a point midway between the olecranon and acromion.

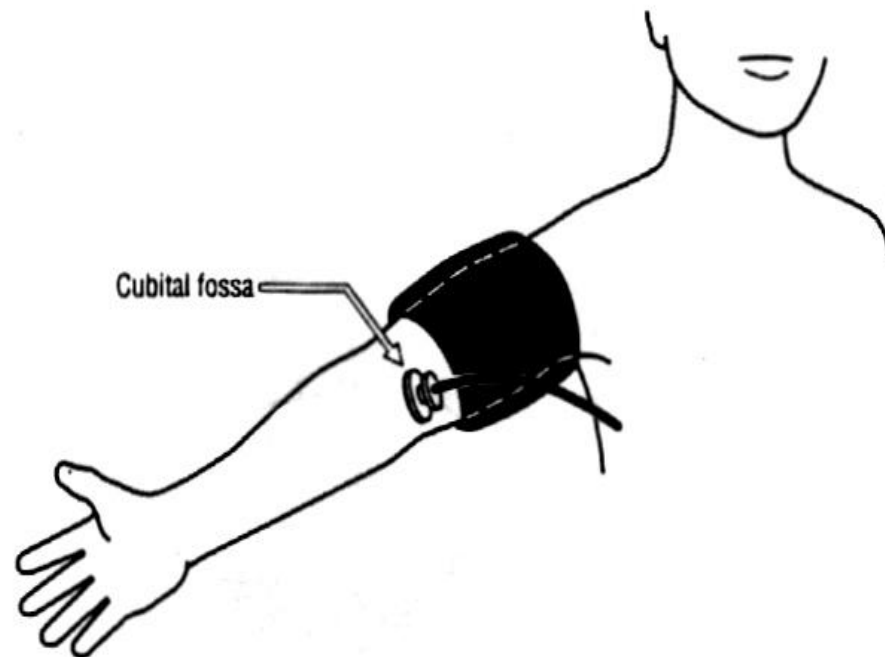


Fig 4. Blood pressure measurement. Blood pressure should be measured with cubital fossa at heart level. The arm should be supported. The stethoscope bell is placed over the brachial artery pulse, proximal and medial to the cubital fossa, below the bottom edge of the cuff.

BP measurement

- Appropriate cuff size
- Methods
 - Auscultatory
 - Oscillometric
 - Ambulatory BP measurements
 - Home measurements

Validation!

BHS: British Hypertension Society

AAMI: American Assoc. for the Advancement of Medical Instrumentation

ESH International Protocol

Recommendations for office BP measurement (SOP)

- Make sure the patient is sitting or relaxed for 3–5 min before beginning BP measurements
- Appropriate cuff size
 - Bladder width **40% of the arm circumference**
 - Bladder length **80–100% of the arm circumference**
- Measure BP: 3-3-last 2
 - 3 times
 - with an interval of 3 min between measurements
 - use the average of the last 2
- The auscultatory method is recommended
 - SBP: Korotkoff sounds Phase I
 - DBP: Korotkoff sounds Phase V
- If oscillometric method is used
 - the model used needs to be validated.
 - If HTN is detected, should be confirmed using the auscultatory method
- Measure BP in both arms at first visit
 - to detect possible differences.
 - In this instance, take the arm with the higher value as the reference

When to measure BP?

- > 3 years of age: All
- < 3 years of age: Under special circumstances
 - Premature infants, LBW
 - Congenital heart disease
 - Recurrent UTI or hematuria or proteinuria
 - Renal or urological diseases
 - Systemic diseases (eg. neurofibromatosis)
 - Solid organ or bone marrow transplantation
 - Drugs which increase BP
 - ..
 - ..

Etiology

- **Primary**
 - Undefined, primary or essential hypertension
 - Associated with metabolic syndrome
 - Associated with obesity without full metabolic syndrome

- **Secondary**
 - Renal
 - Vascular
 - Endocrine
 - Central
 - Iatrogenic

Etiology

- **Renal**

- Renal parenchymal
 - Glomerulonephritides
 - Polycystic kidney disease (PKD)
 - Pyelonephritis
- Obstructive uropathy
- Transporter mutations
 - Gordon syndrome
 - Liddle syndrome

- **Vascular**

- Renovascular
 - Main renal arteries
 - Branch arteries
- Coarctation of aorta
 - Thoracic
 - Abdominal
- Midaortic syndrome
- Vasculopathies

- **Endocrine**

- Adrenal
 - Adrenal adenoma
 - Glucocorticoid responsive aldosteronism (GRA)
 - Apparent mineralocorticoid excess (AME)
 - Congenital adrenal hyperplasia (CAH)
- Thyroid
 - Hyperthyroidism
 - Hypothyroidism
- Parathyroid
 - Associated with hyperparathyroidism
- Pituitary
 - Cushing syndrome
 - Pituitary tumors

- **Central**

- Sympathetic nervous system abnormalities
- Conditions associated with increased intracranial pressure
- Vasomotor center abnormalities

- **Iatrogenous**

- Medications
- Substances (some of which are drugs)

Ingelfinger JR. Etiology of Childhood Hypertension. Comprehensive Pediatric Nephrology. 2008: 665-675 .

Etiology

	Infants ¹	School age	Adolescents
Primary/essential	<1%	15-30	85-95
Secondary	99%	70-85	5-15 ²
Renal parenchymal	20%	60-70	
Renovascular	25	5-10	
Endocrine	1	3-5	
Coarctation of aorta	35	10-20	
Reflux nephropathy	0	5-10	
Neoplastic	4	1-5	
Miscellaneous	20	1-5	

1: Younger than 1 year.

2: Breakdown of causes is generally similar to that for school-age children.

Belsha CW, Flynn JT. Systemic hypertension.
Rudolph's Pediatrics (22nd ed). 2011: 1757-1768.

Evaluation

- History, physical examination
- Is patient hypertensive?
 - Repeated measurements
 - ABPM, home BP measurement
 - White coat, masked HT?
- Target organ damage?
 - Heart (30-40% in primary HTN), kidney, eye, growth, brain
- Associated CV risk factors?
 - Diabetes, elevated lipids, cardiac disease
- Secondary causes?

Symptoms of hypertension

- Headache
- Epistaxis
- Flush
- Visual disturbance
- Vertigo
- Decline of school performance

Clinical history

- History or symptoms of secondary hypertension
 - Perinatal history:
 - oligohydramnios, anoxia, umbilical artery catheterization and renal artery/vein thrombosis
 - Underlying or concurrent diseases
 - Renal or urologic disease, trauma, recurrent urinary tract infections, edema, weight loss, failure to thrive, thirst/polyuria, nocturia and hematuria
 - Cardiac, endocrine, or neurological disease, cold extremities, intermittent claudication, palpitations, sweating, fever, pallor, flushing, muscle weakness, cramps, virilization, primary amenorrhea, male pseudo-hermaphroditism and skin abnormalities
 - Systemic disease (lupus erythematosus)
 - Drug/substance intake:
 - steroids, calcineurin inhibitors, TCAs, decongestants, oral contraceptives, amphetamines and cocaine
- History or symptoms of target organ damage
 - Headache, epistaxis, vertigo, visual impairment, facial palsy, seizures, strokes, low school performance, dyspnea, chest pain, palpitations and syncope

Clinical history

- Risk factors
 - Diabetes mellitus
 - Dyslipidemia
 - Obesity and growth patterns
 - Physical exercise and dietary habits
 - Smoking and alcohol
 - Birth weight and gestational age
 - Snoring and sleep apnea history
- Hypertension onset and management
 - Age at presentation
 - Previous blood pressure measurements
 - Past and current treatment
 - Compliance-adverse effects

Family history

- Family history
 - Hypertension
 - Diabetes
 - Dyslipidemia
 - Cardiovascular disease
 - Hereditary renal disease
 - polycystic kidney disease and Alport syndrome
 - Hereditary endocrine disease
 - adrenal tumors, glucocorticoid-remediable aldosteronism, multiple endocrine neoplasia type 2 and monogenic syndromes of hypertension)
 - Syndromes associated with hypertension (neurofibromatosis)

Clues toward underlying cause

- **Renal disease**
 - Edema, polyuria, nocturia, hematuria,
 - Fatigue, muscle weakness, weight loss, failure to thrive
 - History of oligohydramnios or recurrent UTIs,
 - Family history of renal failure
- **Renovascular disease**
 - Neonatal history of umbilical arterial catheter,
 - Neonatal asphyxia, or episodes of severe hypotension
- **Tumor**
 - Weight loss, flushing, sweating
- **Systemic disease**
 - Skin abnormalities (systemic lupus erythematosus, neurofibromatosis, scleroderma), family history, such as hyperthyroidism

Clues toward underlying cause

- **Clues toward iatrogenic hypertension**
 - Previous medical history
 - Medication:
 - anti-inflammatory agents, decongestants, stimulants (e.g., for attention deficit disorder), tricyclic antidepressants, immunosuppressives, hormonal contraceptives
- **Clues toward essential hypertension**
 - Weight gain and diet, physical activity
 - Smoking/alcohol
 - Family history of cardiovascular disease or diabetes
 - Sleep disturbance (sleep apnea)
- **Important questions at follow-up visits**
 - Medication side effects, such as fatigue (β blockers), cough (angiotensin-converting enzyme [ACE] inhibitors), enuresis (diuretics)
 - Compliance with therapeutic lifestyle changes.
 - Compliance with medication

Possible Physical Signs in Hypertensive Patient

- **Body habitus**
 - Obesity Metabolic syndrome, primary HTN
 - Truncal obesity Cushing syndrome
 - Thinness Hyperthyroidism, pheochromocytoma
 - Short stature CKD—Turner, Williams, or Gordon syndrome
 - Webbed neck Turner or Gordon syndrome
 - Widely spaced nipples Turner syndrome
- **Face**
 - Rounded facies/moon face Cushing syndrome
 - Elfin facies Williams syndrome
 - VIIth cranial nerve palsy Hypertensive encephalopathy
- **Skin**
 - Edema, pale mucous membranes Renal failure
 - Pallor, flushing, diaphoresis Pheochromocytoma
 - Acne, hirsutism, striae Cushing syndrome
 - Acanthosis nigricans Type 2 diabetes mellitus
 - Café-au-lait spots, neurofibromas Neurofibromatosis
 - Butterfly rash SLE
 - Adenoma sebaceum, ash leaf spots Tuberous sclerosis
 - Vasculitis SLE, Henoch-Schönlein nephritis, collagen vascular dis.

Possible Physical Signs in Hypertensive Patient

- | | |
|---|---|
| • Head and neck | |
| – Goiter | Hyperthyroidism |
| • Eyes | |
| – Hypertensive retinal changes | Severe or longstanding HTN |
| – Exophthalmus | Hyperthyroidism |
| – External ocular nerve palsies | Severe HTN, hyperthyroidism |
| • Throat | |
| – Adenotonsillar hypertrophy | Sleep apnea |
| • Cardiovascular system | |
| – Tachycardia | Hyperthyroidism, pheochromocytoma, neuroblastoma, primary HTN |
| – Apical heave, enlarged heart | Left ventricular hypertrophy |
| – Cardiac friction rub | Pericarditis due to SLE, uremia, or collagen vascular disease |
| – Loss of foot pulses, leg BP more than 10 mm Hg below arm BP, heart murmur | Coarctation of aorta |
| – Edema, heart murmur | Heart failure |
| – Abdominal bruit | Renal artery stenosis |

Possible Physical Signs in Hypertensive Patient

- **Abdomen and urogenital system**

- Abdominal mass, palpable kidneys
- Hepatomegaly
- Flank tenderness
- Ambiguous genitalia, virilization

Wilms tumor, neuroblastoma, pheochromocytoma,
polycystic kidney disease,
severe hydronephrosis, multicystic-dysplastic kidney
Autosomal recessive polycystic kidney disease, heart failure
Acute glomerulonephritis or obstruction, pyelonephritis
Congenital adrenal hyperplasia

- **Musculoskeletal system**

- Joint swelling
- Rickets
- Brachydactyly
- Muscle weakness

SLE, collagen vascular disease
Chronic renal failure
Hypertension brachydactyly syndrome, Gordon syndrome
Hyperaldosteronism, Liddle syndrome

Evaluation

- History, examination
- Is patient hypertensive?
 - Repeated measurements
 - ABPM, home BP measurement
 - White coat, masked HT?
- Target organ damage?
 - Heart, kidney, eye, growth, brain
- Associated CV risk factors?
 - Diabetes, elevated lipids, cardiac disease
- Secondary causes?

ABPM

ambulatory BP monitoring

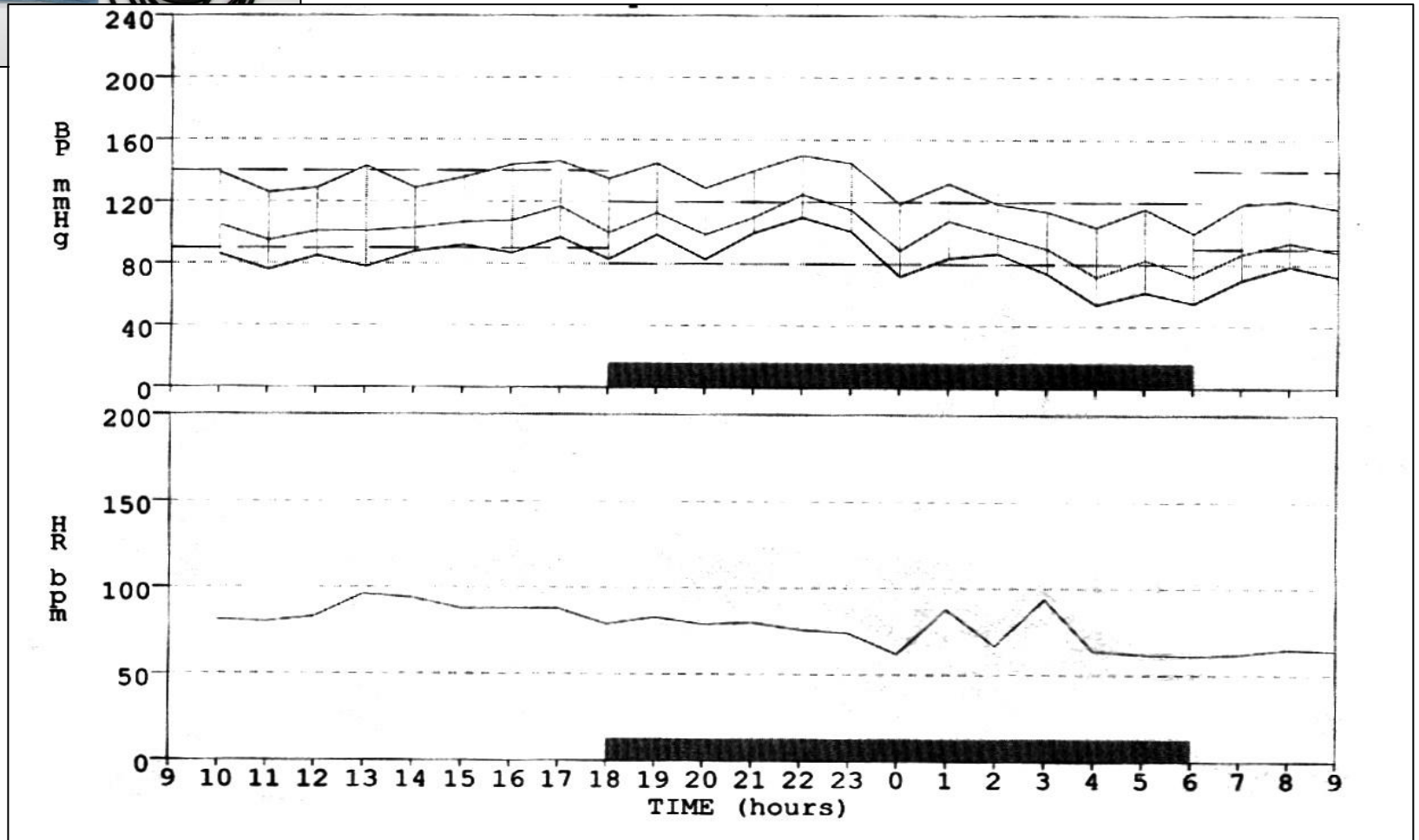


Table 1. Pros and Cons of Oscillometric Versus Auscultatory Ambulatory BP Devices

Oscillometric	Auscultative
Pros: <ul style="list-style-type: none">• Easier to use• Fewer erroneous readings	Pros: <ul style="list-style-type: none">• Diastolic BP may be defined as 4th or 5th Korotkoff sound• Systolic and diastolic pressures are measured in a similar fashion to resting, casual BP
Cons: <ul style="list-style-type: none">• Systolic and diastolic pressures are calculated, not measured• Calculation formulas are proprietary	Cons: <ul style="list-style-type: none">• No normative data available• More difficult to use• Fewer machines to choose• No consensus on lower age at which Korotkoff sounds are audible or accurate

BP indicates blood pressure.

Indications for ABPM

- During the process of diagnosis
 - Confirm hypertension before starting antihypertensive drug treatment to avoid treatment of white-coat hypertension
 - Target organ damage (LVH and microalbuminuria) and office BP normal (masked hypertension)
 - DM1 and DM2
 - CKD
 - Renal, liver or heart transplant
 - Severe obesity with or without sleep-disordered breathing
 - Hypertensive response during the treadmill test
 - Discrepancy between office BP and home BP
- During antihypertensive drug treatment
 - Evaluate for apparent drug-resistant hypertension
 - Assessment of BP control in children with target organ damage
 - Symptoms of hypotension

Table 2. Conditions in Which ABPM May Be Particularly Helpful*

Condition	Relevance of ABPM
Secondary hypertension	Elevated load, abnormal dipping and variability
Chronic kidney disease	Prevalence of hypertension, masked hypertension, association with target-organ changes and disease progression
Types 1 and 2 diabetes mellitus	Abnormal circadian variation, association with microalbuminuria and vascular changes
Obesity	Masked hypertension, correlation between BMI and hypertension severity, abnormal dipping, association with target-organ damage
Sleep apnea	Hypertension severity, abnormal circadian variation
Genetic syndromes Neurofibromatosis type 1 Turner syndrome Williams syndrome	Abnormal BP patterns indicating secondary cause of hypertension, especially renal artery stenosis and aortic coarctation
Treated patients with hypertension	Response to antihypertensive medications and/or lifestyle changes
Hypertension research	Reduction in subject number in drug trials

ABPM indicates ambulatory blood pressure monitoring; BMI, body mass index; and BP, blood pressure.

Pediatric ABPM Reference Data

Age (years)	Boys						Girls					
	Day			Night			Day			Night		
	75th	90th	95th	75th	90th	95th	75th	90th	95th	75th	90th	95th
5	116/76	120/79	123/81	99/59	103/62	106/65	114/77	118/80	121/82	100/61	105/66	108/69
6	116/76	121/79	124/81	100/59	105/63	108/66	115/77	120/80	122/82	101/61	106/65	110/68
7	117/76	122/80	125/82	101/60	106/64	110/67	116/77	121/80	123/82	102/60	107/65	111/67
8	117/76	122/80	125/82	102/60	108/64	111/67	117/76	122/80	124/82	103/60	108/64	112/67
9	118/76	123/80	126/82	103/60	109/64	112/67	118/76	122/80	125/82	103/59	109/64	112/67
10	119/76	124/80	127/82	104/60	110/64	113/67	119/76	123/79	126/81	104/59	110/64	113/67
11	121/76	126/80	129/82	105/60	111/64	115/67	120/76	124/79	127/81	105/59	110/63	114/66
12	123/76	128/80	132/82	107/60	113/64	116/67	121/76	125/80	128/82	105/59	110/63	114/66
13	126/76	131/80	135/82	109/60	115/64	119/67	122/77	126/80	129/82	106/59	111/63	114/66
14	129/77	134/80	138/82	112/61	118/64	121/67	123/77	127/80	130/82	106/59	111/63	114/65
15	132/77	137/81	141/83	114/61	120/64	123/66	124/77	128/80	130/82	107/59	111/63	114/65
16	135/78	140/81	144/84	117/61	123/64	126/66	124/77	129/80	131/82	107/59	111/63	114/65
Height (cm)	Boys						Girls					
	Day			Night			Day			Night		
	75th	90th	95th	75th	90th	95th	75th	90th	95th	75th	90th	95th
120	116/77	122/80	125/82	99/58	103/61	106/63	114/77	118/80	120/82	99/60	103/63	106/65
125	117/76	122/80	125/82	100/58	105/61	108/63	115/77	119/80	121/82	100/60	104/63	107/66
130	117/76	122/80	126/82	101/59	106/62	110/64	116/76	120/80	122/82	101/59	106/63	108/66
135	117/76	123/80	126/82	102/59	108/63	111/65	116/76	120/80	123/82	102/59	107/63	109/66
140	118/76	123/80	126/82	104/60	109/63	113/65	117/76	121/80	124/82	103/59	108/63	110/66
145	119/76	124/79	127/81	105/60	111/64	114/66	118/76	123/80	125/82	103/59	109/63	112/66
150	120/76	125/79	128/81	106/60	112/64	116/66	119/76	124/80	127/82	104/59	110/63	113/66
155	122/76	127/79	130/81	107/60	113/64	117/66	121/76	125/80	128/82	106/59	111/63	114/66
160	124/76	129/79	133/81	108/60	114/64	118/66	122/76	126/80	129/82	106/59	111/63	114/66
165	126/76	132/80	135/82	110/60	116/64	119/66	123/77	127/80	130/82	107/59	112/63	114/66
170	128/77	134/80	138/82	112/61	117/64	121/66	124/77	128/80	131/82	108/61	112/67	115/71
175	130/77	136/81	140/83	113/61	119/64	122/66	125/78	129/81	131/82	109/59	113/63	115/66
180	132/77	138/81	142/83	115/61	120/64	124/66	N/A	N/A	N/A	N/A	N/A	N/A
185	134/78	140/81	144/84	116/61	122/64	125/66	N/A	N/A	N/A	N/A	N/A	N/A

Soergel et al. J Pediatr 1997;130: 178-184.
Wühl et al. J Hypertens 2002;20: 1995-2007.

Requirements for a satisfactory ABPM

- **Basic requirements**
 - Patients must be capable of understanding the procedure and coping with the device
 - ABPM should be performed preferably on a routine working day
 - Repeat ABPMs should be on like days (routine working or recreational)
- **Fitting the monitor**
 - Select frequency of measurement—*15–30 min for day and night*
 - Inactivate measurement LCD display
 - Apply cuff to non-dominant arm
 - Choose appropriate cuff
 - Centre of bladder should be over the brachial artery
 - Place cuff on bare arm with tubing passing upwards around patient's neck to be connected to the monitor on the waist
 - Perform trial measurement to check working and familiarize patient with the monitor

Requirements for a satisfactory ABPM

- **Advice to the patient**

- Procedure should be explained
- Instructions printed on a diary card on which time of drug intake, time of going to bed and rising and any symptoms may be recorded
- Patients should be told to follow their usual daily activities but to remain still during measurement with the arm relaxed at heart level
- Instruct patient to place monitor on the bed or beneath the pillow at night
- Warn patient not to take a shower or bath
- Advise patient not to drive but if this is necessary to stop if possible during measurement
- Mark the brachial artery so that if the cuff becomes loose the patient can refit it
- Instruct patient how to switch off the monitor in case of malfunctioning, such as repeated inflation

Requirements for a satisfactory ABPM

- **Removing the monitor**
 - Usually removed by operator after 24–25 h but patients can be instructed to remove and switch off the monitor and send it to the operator's centre
 - Connect the monitor to computer and download the data
 - If minimum requirement not met, ABPM should be repeated though sub-optimal data can be helpful.

“Quality criteria” for ABPM

- 24-h recording with at least 70% of expected measurements
- At least 20 valid awake and 7 valid asleep measurements
- At least two valid daytime and one valid night-time measurement per hour for research purposes

ABPM

- Systolic BP, diastolic BP, mean arterial pressure (MAP) and heart rate
- Mean, min. and max. values for daytime, nighttime and 24h
- Load: percentage of BP values > 95th pct

Table 2. Suggested Schema for Staging of Ambulatory BP Levels in Children

Classification	Clinic BP*	Mean Ambulatory SBP†	SBP Load, % ^{70,75}
Normal BP	<95th percentile	<95th percentile	<25
WCH	>95th percentile	<95th percentile	<25
Masked hypertension	<95th percentile	>95th percentile	>25
Prehypertension	>95th percentile	<95th percentile	25–50
Ambulatory hypertension	>95th percentile	>95th percentile	25–50
Severe ambulatory hypertension (at risk for end-organ damage)	>95th percentile	>95th percentile	>50

Modified from Lurbe et al,⁷⁴ with permission.

BP indicates blood pressure; SBP, systolic blood pressure.

*Based on the National High Blood Pressure Education Program Task Force Standards.

†Based on ABPM values of Soergel et al or the smoothed values of Wühl.

Table 3. Suggested Revised Schema for Staging of Ambulatory BP Levels in Children

Classification	Office BP*	Mean Ambulatory SBP or DBP†‡	SBP or DBP Load, %†§
Normal BP	<90th %tile	<95th %tile	<25
White coat hypertension	≥95th %tile	<95th %tile	<25
Prehypertension	≥90th %tile or >120/80 mm Hg	<95th %tile	≥25
Masked hypertension	<95th %tile	>95th %tile	≥25
Ambulatory hypertension	>95th %tile	>95th %tile	25–50
Severe ambulatory hypertension (at risk for end-organ damage)	>95th %tile	>95th %tile	>50

%tile indicates percentile; BP, blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

*Based on National High Blood Pressure Education Program Task Force normative data.^{101a}

†Based on normative pediatric ABPM values in Appendix Tables A1 through A4.

‡For either the wake or sleep period of the study, or both.

§For patients with elevated load but normal mean ambulatory BP and office BP that is either normal (<90th percentile) or hypertensive (≥95th percentile), no specific ambulatory BP classification can be assigned based on current evidence and expert consensus. These “unclassified” patients should be evaluated on a case-by-case basis, taking into account the presence of secondary hypertension or multiple cardiovascular risk factors.

||Some clinicians may prefer the term *sustained hypertension* rather than *ambulatory hypertension*.

“Classical” BP Classification

Classification	Casual BP	ABPM*
Confirmed normotension	normal	normal
White coat hypertension	> 95th pct	normal
Masked hypertension	normal	> 95th pct
Confirmed hypertension	> 95th pct	> 95th pct

* Time averaged 24-hour mean arterial pressure

Home BP monitoring

- Methodological aspects
 - Measured daily on at least 3–4 days, preferably on 7 consecutive days in the mornings as well as in the evenings
 - Measured in a quiet room, with the patient in the seated position, back and arm supported, after 5 min of rest
 - Two measurements per occasion taken 1–2 min apart
 - Home blood pressure is the average of these readings, with exclusion of the first monitoring day
- Clinical indications for use
 - All patients receiving antihypertensive medication
 - Suspicion of white-coat hypertension
 - Conditions where strict BP control is mandatory (high-risk patients)
 - Clinical trials

TABLE 12. Systolic and diastolic home blood pressure values (SBP/DBP)

Height (cm)	Percentiles for boys (<i>n</i> = 347)		Percentiles for girls (<i>n</i> = 420)	
	50th	95th	50th	95th
120–129	105/64	119/76	101/64	119/74
130–139	108/64	121/77	103/64	120/76
140–149	110/65	125/77	105/65	122/77
150–159	112/65	126/78	108/66	123/77
160–169	115/65	128/78	110/66	124/78
170–179	117/66	132/78	112/66	125/79
180–189	121/67	134/79	114/67	128/80

Stergiou GS, et al.
Home blood pressure normalcy in children and adolescents:
the Arsakeion Schoolstudy. J Hypertens 2007; 25:1375–1379.

Laboratory tests

- First line
 - CBC
 - Urinalysis, urine culture
 - Biochemistry
 - Creatinine, urea, electrolytes, uric acid
 - Cholesterol, triglycerides, fasting plasma glucose
 - Renal USG
 - Echocardiography
 - Albuminuria, proteinuria

Laboratory tests

- Second line (in specific conditions)
 - Renin-aldosteron
 - Urinary and plasma catecholamines
 - Urinary free cortisol, plasma cortisol, ACTH, 24 hour urinary free cortisol
 - Thyroid functions
 - Molecular genetic studies

 - Doppler US
 - Renal scintigraphy
 - Voiding CUG
 - CT, MR angiography
 - Renal vein renin, biopsy, MIBG,
 - Cardiac catheter

Target organ damage



- Cardiovascular
 - Left ventricular hypertrophy (LVMI)
 - Left atrial dilation ↑
 - Carotis intima-media thickness ↑
 - Radial artery compliance ↓
 - Atherosclerosis
- Renal
 - Microalbuminuria
- Ocular
 - Retinopathy
- Central NS
 - ischemic stroke, cerebral hemorrhage
 - convulsion

Criteria to define hypertension-induced organ damage

- LVH
 - LVMI or RWT \geq 95th percentile by age and sex
- Carotid intima thickness
 - cIMT \geq 95th percentile by age and sex
- Pulse wave velocity (PWV)
 - PWV \geq 95th percentile by age and sex
- Kidney
 - Albuminuria
 - ACR: >30 mg/g creatinine or >3 mg/mmol creatinine)
 - Even proteinuria
 - ACR: >300 mg/g creatinine or >30 mg/mmol creatinine)
 - Or 24 h urinary protein excretion: >200 mg/m²/day

Clinical indication	Blood pressure goal
Persistent hypertension despite therapeutic lifestyle modification	<95 th 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

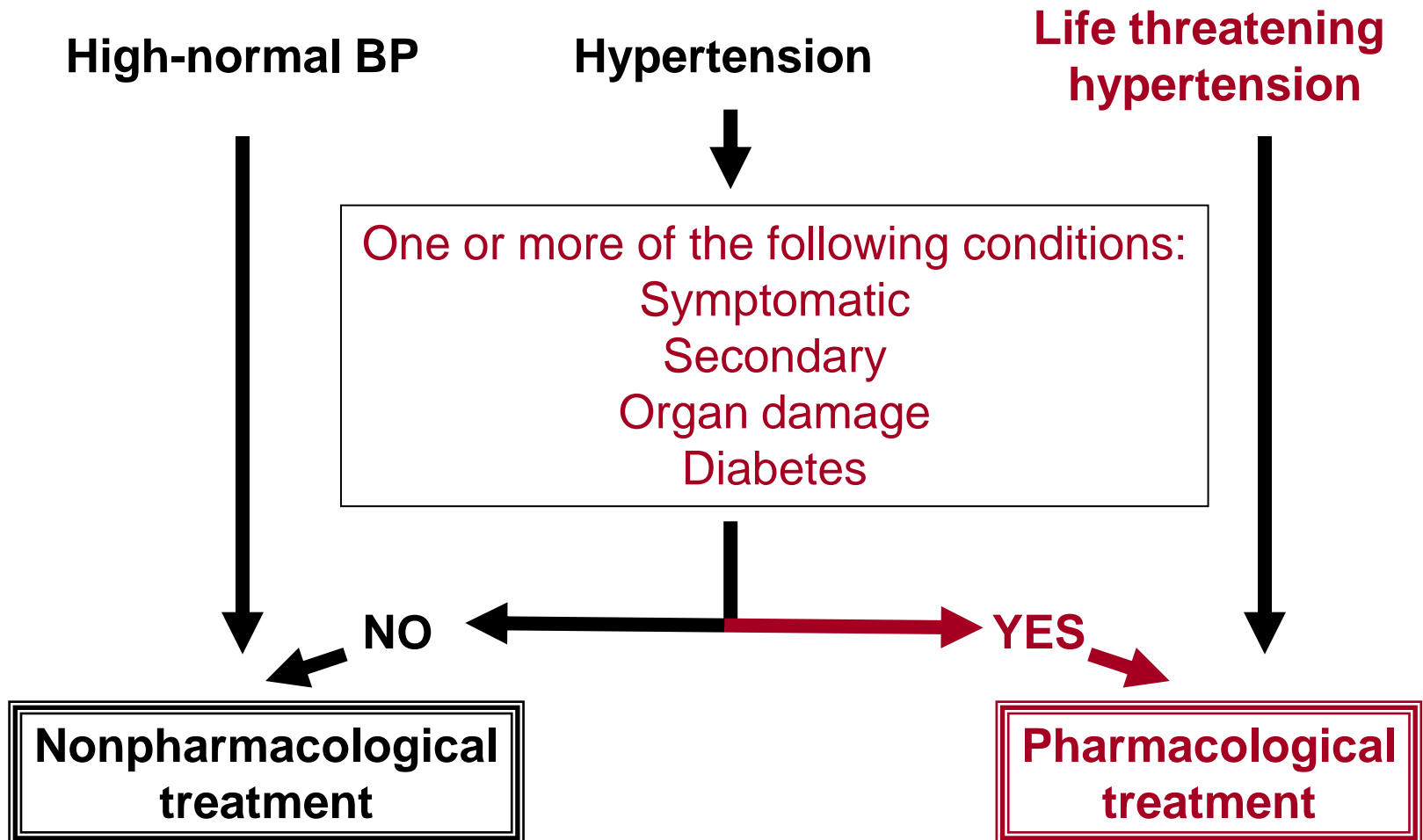
Ferguson MA, Flynn JT.
Rational use of antihypertensive medications in children.
Pediatr Nephrol 2014; 29: 979–988.

BP Goal

ESH Guideline, 2016

- General hypertensive population
 - Blood pressure goal <95th percentile is recommended
<90th percentile should be considered
- DM1 and DM2
 - Blood pressure goal <90th percentile is recommended
<75th percentile is recommended in children with nonproteinuric CKD
<50th percentile is recommended in children with proteinuric CKD
- Children with CKD
 - Blood pressure goal <75th percentile is recommended in children with nonproteinuric CKD
<50th percentile is recommended in children with proteinuric CKD

When to initiate antihypertensive treatment



Life style recommendations to reduce high BP

- General recommendations
 - Implement the **behavioral changes** (physical activity and diet) tailored to individual and family characteristics
 - **Involve the parents/family** as partners in the behavioral change process
 - Encourage **smoke-free** environment throughout all stages of life, including discouraging maternal smoking
 - Provide **educational support** and materials
 - Establish **realistic goals**
 - Develop a health-promoting **reward system**

- **BMI**

- BMI <85th percentile : maintain BMI to prevent overweight
- BMI 85–95th percentile : weight maintenance (younger children) or gradual weight loss in adolescents to reduce BMI to <85th percentile
- BMI >95th percentile : gradual weight loss (1–2 kg/month) to achieve value <85th percentile

- **Physical activity**

- Children and youth aged 5–17 years should accumulate **at least 60 min of moderate-to-vigorous-intensity** physical activity daily.
- Amount of physical activity greater than 60 min provides additional health benefits
- Most of the daily physical activity should be **aerobic. Vigorous-intensity activities** should be incorporated, including those strengthening muscle and bone, at least three times per week
- **Avoid more than 2 h daily of sedentary activities**
- Competitive sports participation should be limited only in the presence of uncontrolled stage 2 hypertension

- **Diet**

- Avoid intake of excess sugar, excess soft drinks, saturated fat and salt and recommend fruits, vegetables and grain products
- Limit salt intake

How to initiate antihypertensive treatment

Particular conditions
Stage 2
Chronic kidney disease
Secondary



All hypertensives

Monotherapy
(low dose
4-8 w)

No response



Monotherapy
(full dose)

No response

Side effects



Switch
drug

No response



Combination
therapy

Antihypertensive treatment

- Efficacy
- Follow-up studies?
- Comparison?
- Indications
- Side effects, contraindications
- Combination
- Dose
 - ESH Guideline. J Hypertens 2016
 - Ferguson MA, Flynn JT. Pediatr Nephrol 2014; 29: 979–988.

Antihypertensive agents with efficacy and safety studies in children and adolescents

Class	Efficacy studies
Diuretics	Clorthalidone, HCZT
β-blockers	Atenolol, Metoprolol, Propanolol
CCB	Amlodipine, Felodipine, Isradipine
ACEi	Captopril, Enalapril, Fosinopril, Lisinopril, Quinapril, Ramipril
ARB	Candesartan, Irbesartan, Losartan, Valsartan

Antihypertensive class	Recommended	Contraindicated
Diuretics potassium-sparing	Hyperaldosteronism	Chronic renal failure ^a Competitive athletes
Thiazide and thiazide-like diuretics	Chronic renal failure Corticosteroid-induced HTN	Competitive athletes Diabetes
Diuretics loop-acting	Congestive heart failure	
Beta-adrenergic blockers	Coarctation of aorta Congestive heart failure Migraine	Bronchial asthma ^a Diabetes Competitive athletes Psoriasis
Calcium channel blockers	Posttransplantation Migraine Coarctation of aorta	Congestive heart failure
ACEi	Chronic kidney disease Diabetes mellitus Microalbuminuria Congestive heart failure Obesity-linked primary HTN	Bilateral renal artery stenosis ^a Renal artery stenosis in solitary kidney ^a Hyperkalemia ^a Pregnancy ^a Females of child-bearing potential should use reliable contraception
ARB	Chronic kidney disease Diabetes mellitus Microalbuminuria Congestive heart failure Obesity-linked primary HTN	Bilateral renal artery stenosis ^a Renal artery stenosis in solitary kidney ^a Hyperkalemia ^a Pregnancy ^a
Intravenous vasodilators	Life-threatening conditions	

ACEi, angiotensin-converting enzyme inhibitor; ARB, AT1 blockers; HTN, hypertension.

^aAbsolute contraindication.

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

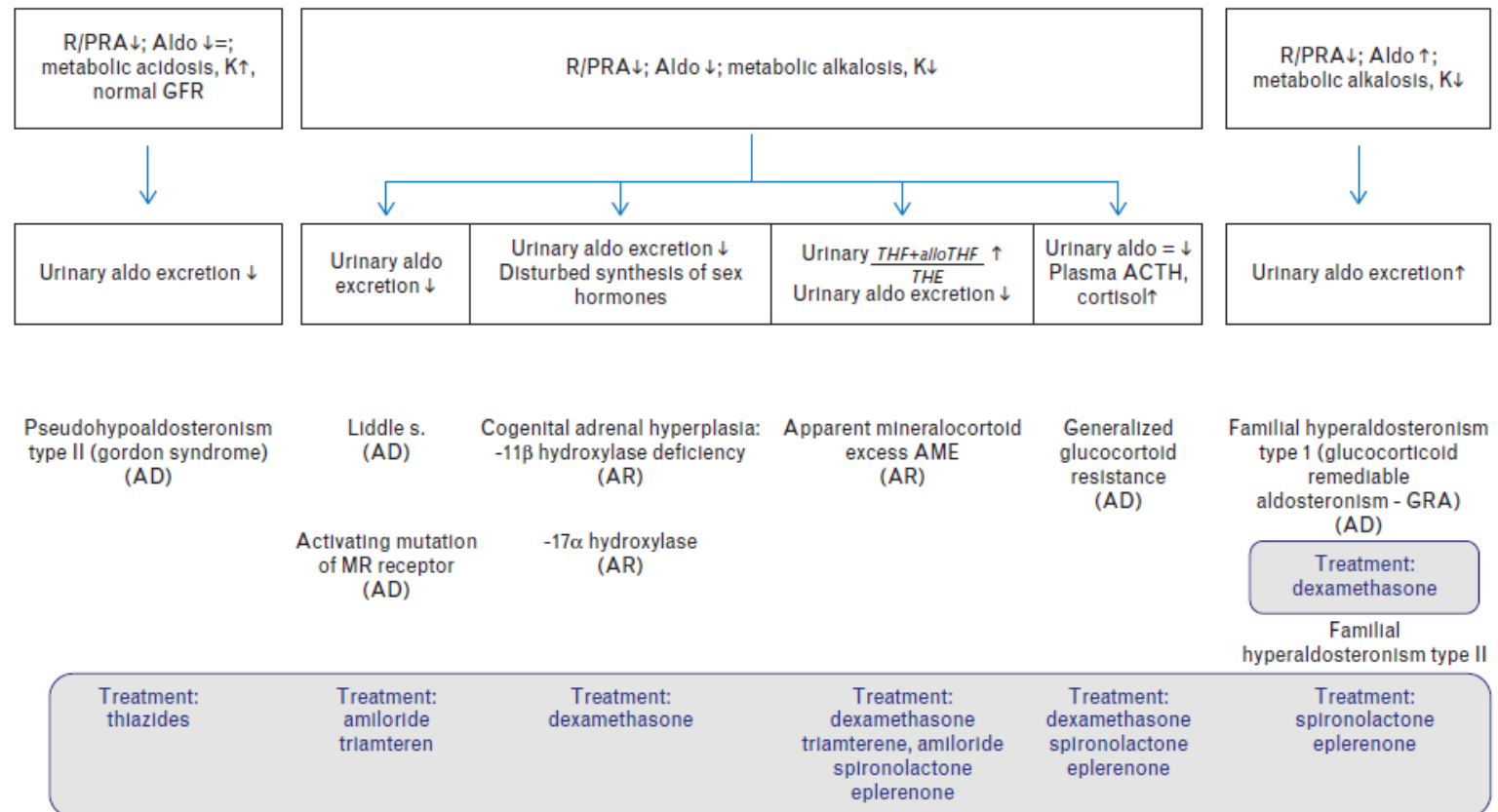
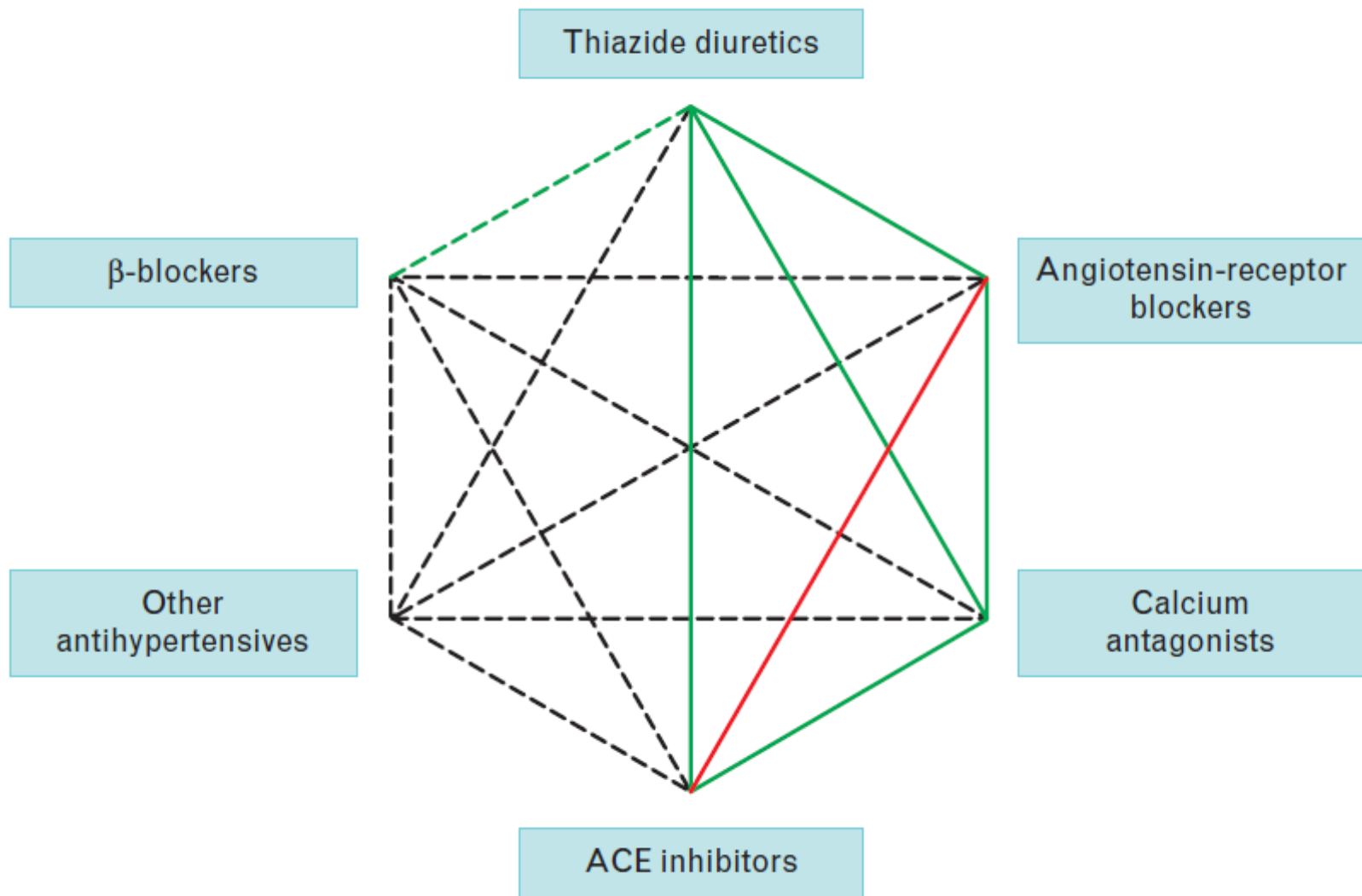


FIGURE 4 Mendelian causes of hypertension. Metabolite profile and recommended treatment. Diagnostic algorithm in low plasma renin activity hypertension and genetic testing. Ratio of urinary THF + alloTHF/THE, normal less than 1.3, apparent mineralocorticoid excess 5–10-fold higher. Shaded area corresponds to the recommended treatment. ACTH, adrenocorticotropic hormone; AD, autosomal dominant; Aldo, aldosterone; alloTHF, allotetrahydrocortisol; AR, autosomal recessive; GFR, glomerular filtration rate; GRA, glucocorticoid remediable aldosteronism; PRA, plasma renin activity; R, rennin; THE, tetrahydrocortisone; THF, tetrahydrocortisol.



Green/continuous: preferred. Green/dashed: useful (with some limitations).

Black/dashed: possible but less well tested. Red/continuous: not recommended.

Only dihydropyridines to be combined with β -blockers. Thiazides + beta-blockers increase risk of new onset diabetes mellitus. ACE + ARBS combination discouraged.

Mancia G, et al., Task Force Members.

2013 ESH/ESC Guidelines for the management of arterial hypertension.

J Hypertens 2013; 31:1281–1357.

Long-term follow-up

- **Initial frequent** follow up visits to monitor
 - BP control, organ damage
 - Side effects of treatment
 - Other reversible risk factors
- **Once BP stable and in target range**, frequency of visits can be reduced
- **Home** monitoring of BP or 24 hour **ABPM** can facilitate follow up assessments
- Dependent on the **underlying cause** of hypertension, further investigative procedures may be indicated to monitor success of surgical intervention or medical treatment

Summary

- Definition
 - Office, ABPM, home BP measurement
 - Normative data
 - ESH Guideline 2016
- Etiology & Evaluation
 - Medical history, physical examination
 - Investigations
 - Target organ damage
- Management of HTN
 - BP goal
 - Life style recommendations
 - Antihypertensive drugs