Hypertension in Children and Young Adults

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KEYWORDS

• Hypertension • Blood pressure • Adolescence • Pediatric • Obesity • Left ventricle • Haemodynamics

KEY POINTS

- The prevalence of primary hypertension continues to increase across childhood populations.
- Secondary hypertension remains the predominant cause of hypertension in young children, in whom underlying kidney disease is the most common pathology.
- Hypertension-mediated organ damage occurs during childhood and prompt diagnosis and appropriate management is important.
- Out-of-office blood pressure monitoring, preferably by 24-h ambulatory blood pressure monitoring is essential for the diagnosis and management of hypertension.
- The Dietary Approach to Stop Hypertension diet, weight control, and increased physical activity are central to the management of hypertension.

INTRODUCTION

Hypertension affects over a billion adults worldwide and is one of the leading causes of premature death.[1] In younger children, most hypertension is secondary but primary hypertension (PH), particularly during adolescence, continues to steadily increase in its prevalence over the past 2 to 3 decades. PH is now the predominant form of hypertension diagnosed in adolescents, in large part due to the epidemic of obesity.[2] This article reviews the epidemiology, diagnosis, and management of hypertension in children and young adults, with a focus on aspects that have not been reviewed recently including global perspective, hemodynamic determinants, and challenges in the provision of care of childhood and adolescent hypertension.[3–5]

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Prevalence

A recent study on the global prevalence of pediatric hypertension included a meta-analysis of 47 studies, covering five continents and data spanning 25 years from 1990 to 2014.[6] The pooled prevalence was 4.0% [95% confidence interval [CI] 3.3%–4.8%], with increasing prevalence over the reported period.[6] Prevalence of elevated blood pressure (BP) (previously known as prehypertension and in Europe known as high normal BP), was 9.7% [7.3%–12.4%]. A strength of this study was the inclusion of only studies in which office BP had been measured on three separate occasions. It is recognized that a lower prevalence of elevated BP is observed if BP is measured repeatedly on more than one visit; this is in keeping with various Clinical Practice Guidelines.[7–11] However, given the practical challenges repeated visits pose, particularly when conducting a research study, many studies report measurements performed during a single visit.

Studies from Australia, Canada, and central Europe published following the meta-analysis by Song and colleagues[6] corroborate its findings, reporting prevalence at 3.1%, 4.5%, and 6%, respectively.[6,12–14] The reported prevalence of hypertension has been affected following a change in the diagnostic threshold as per the 2017 AAP Clinical Practice Guideline.[10] Analysis of a large US cohort from the National Health and Nutrition Survey (NHANES) found that the application of these guidelines increased the prevalence from 2.7% to 5.5%.[15] Similarly, a Spanish study reported an increase in the prevalence of hypertension from 6.6% when using 2016 European Society of Hypertension (referred to as "2016 ESH") guidelines to 10.6% under the 2017 American Academy of Pediatrics (referred to as "2017 AAP") guidelines.[16] The 2017 AAP guideline change should therefore be kept in mind when interpreting data regarding the prevalence of childhood hypertension.

Hypertension in Low- and Middle-Income Countries

The majority of adults with hypertension live in low- and middle-income countries (LIMCs), with one in three estimated to be hypertensive.[17] Data regarding pediatric hypertension prevalence in LIMCs is mixed: the Middle East, South America, China, India, and Nigeria were represented in the meta-analysis by Song and colleagues, with prevalence varying from 1.1% (India, 1994) to 12.8% (Nigeria, 2017).[6,18,19] Two recent studies in Sub-Saharan Africa using repeated BP measurements found a prevalence of 3.1% in rural Uganda and 1.6% in rural Cameroon using 2016 ESH and the so-called, 2004 Fourth Report guidelines.[20,21] In contrast, a Tanzanian study observed a much higher prevalence of 10.2% following three repeated measurements.[9] It remains unclear whether the significant variation in prevalence across studies is primarily because of inherent differences in population and lifestyle factors, or methodological differences pertaining to included age range, definition of hypertension, or sampling bias. With these potential confounders, it remains difficult to compare the true prevalence of hypertension in childhood across different global regions to monitor trends and ultimately focus resources.

Genetics

Monogenic forms of hypertension remain extremely rare and have been well described elsewhere.[22] It has long been known that PH has a substantial polygenic component, with twin studies over the past 30 years in children and adults confirming significant heritability.[23] A recent meta-analysis of twin studies on familial aggregation in childhood BP, suggested that approximately 70% of the BP variability was explained by a shared environment, whereas genetics comprised a relatively modest 25%.[24]

Genome-wide association studies (GWAS) allow simultaneous comparison of hundreds of thousands of gene variants and have dramatically advanced the identification of the specific gene variants determining hypertension. In 2011, a GWAS consortium collated the known 29 genome-wide significant variants, developing the first genetic risk score for hypertension; there are now over 1000 loci of interest.[25,26] A study based on TwinsUK and UK Biobank cohorts found pulsatile and systolic components of BP showed a much higher heritability than diastolic and mean arterial pressure.[27] This is an interesting finding when paired with hemodynamic observations regarding pulsatile components of BP contributing disproportionately to hypertension in childhood. To date, the association between reported loci and BP during childhood has not been tested. Overall, although significant advances in this area are expected in the coming decades, there is currently no role in clinical practice for genetic testing in PH.

Excess Weight and Hypertension

Obesity is well established as an independent risk factor for hypertension.[8,28] In a Canadian study where BP was measured at mean ages of 12.8, 15.2, and 17 years, an increase in 1 body mass index (BMI) unit was associated with an increase of 0.7 mm Hg systolic blood pressure (SBP).[29] Prevalence of hypertension in those with overweight and obesity has been estimated between 15.3% and 40%, although studies again vary in the number of BP measurements performed and definition of hypertension.[6,8,14,30] However, the relationship between excess weight and BP is not observed in all populations. Data from Tanzania and South Africa report a low prevalence of obesity within their hypertensive cohorts.[9,31] Furthermore, an analysis of changes in BMI and BP from 1974 to 1993 in subjects of the Bogalusa Heart Study showed that the increased rate of obesity from 6% to 17% during this time was not associated with an increase in SBP and DBP.[32] These findings imply that obesity-independent processes are also important in the development of PH in childhood.

Obesity and hypertension have both independent and summative effects on left ventricular remodeling. A decrease in abdominal obesity and an increase in lean body mass are the main predictors of left ventricular hypertrophy (LVH) regression in hypertensive adolescents.[33] The main metabolic abnormalities associated with excess weight are hyperinsulinaemia and insulin resistance. This results from a pro-inflammatory state established by excess adipose tissue, in particular visceral as opposed to subcutaneous adipose tissue.[34] Hyperinsulinaemia is known to result in sympathetic nervous system (SNS) activation and several cross-sectional and epidemiological studies have observed higher heart rate (HR), stroke volume (SV), or cardiac output (CO) in those with excess weight.[30] These observations have underpinned the hyperdynamic state theory.

Hemodynamics

The predominant phenotype of hypertension in children, adolescents, and young adults is isolated systolic hypertension (ISH), characterized by a raised pulse pressure (PP), whereas hypertension diagnosed in 30–50-year-olds is predominantly isolated diastolic hypertension (IDH) and systo-diastolic hypertension (SDH), before ISH becomes the main phenotype with increasing age.[30,35,36] These changing phenotypes are thought to be driven by age-related changes in the arterial tree, a phenomenon less likely to be occurring in hypertensive children during the first two decades of life.

Support for a ‘‘hyperdynamic state” has emerged following observations that CO or its component, HR, and SV are raised in hypertensive children and young adults.[8,30,37] These data suggest that instead of a “vascular”-driven process, a “cardiac”-driven process is dominant in at least a subset of children and young adults with

hypertension. Increased SNS activity is proposed as the pathophysiological link between obesity, PH, increased CO, and altered ventricular ejection dynamics.[34,38] Recent evidence suggests a presence of distinct hemodynamic phenotypes within PH, eg, males tending toward a "cardiac" phenotype and females tending toward "vascular."[39] It remains interesting to consider that the earliest hemodynamic changes may be cardiac driven and that these promote vascular remodeling which over time switches the phenotype to more of a vascular phenotype.[40] Arguments for and against the "hyperdynamic state" theory are subject to ongoing debate in the literature and the interested reader is directed to recent reviews on the subject.[41,42] **Fig. 1** summarizes important hemodynamic relationships and a proposed pathophysiological model of factors leading to hypertension in young people.[27,28,36,41]

Studies measuring detailed hemodynamic parameters in healthy weight hypertensive and obese hypertensive individuals compared with normotensive subjects are needed. Further, studies to investigate the effect of different antihypertensive medications on these emerging distinct hypertensive phenotypes may help develop a more logical approach to the management of childhood hypertension.

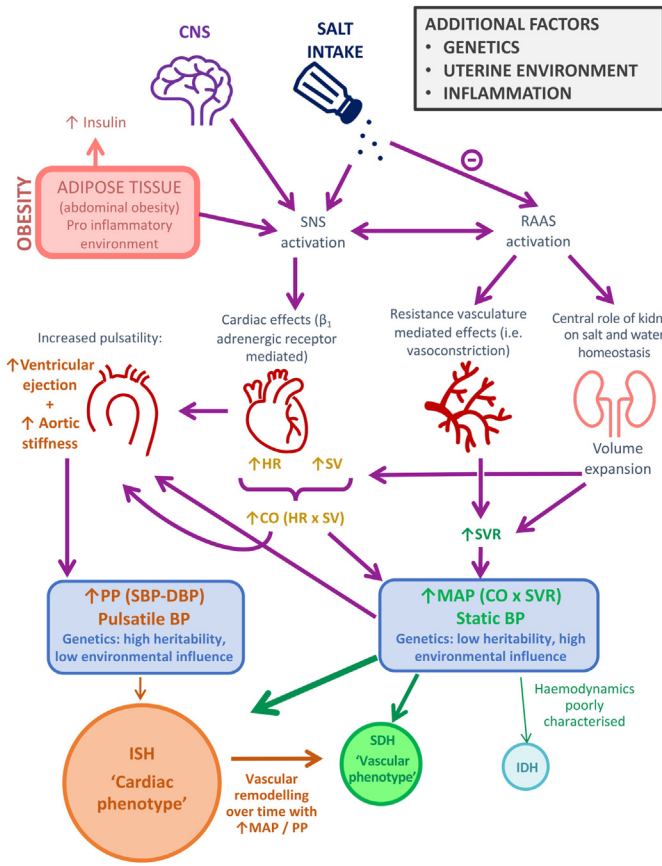

Fig. 1. Key pathophysiological processes involved in raised BP–simplified diagram. CNS, central nervous system; CO, cardiac output; HR, heart rate; HTN, hypertension; IDH, isolated diastolic hypertension; MAP, mean arterial pressure; PP, pulse pressure; RAAS, renin angiotensin aldosterone system; SDH, systo-diastolic hypertension; SNS, sympathetic nervous system; SV, stroke volume; SVR, systemic vascular resistance.

Blood Pressure Tracking

Tracking refers to the tendency for an individual with normal BP to increase with time such that it remains around the percentile of initial measurement. Robust data provide evidence of tracking of BP from childhood to adult life, with correlation coefficient estimated at 0.38 for SBP and 0.28 for DBP.[43] These data suggest that children with high BP have a high risk for future hypertension. Correlation increased with age, into adolescence, and in the presence of obesity.[43]

Intrauterine environment, including both fetal under and overnutrition, have been shown to influence BP in early life.[44] Fetal "programming" is likely to interact with childhood weight trajectory, environmental and genetic factors to influence BP trajectory, and risk of cardiovascular disease as an adult.[44] Hypertension in adulthood is more likely with sustained rather than transient high BP in childhood.[45] In the Bogalusa cohort, the presence of LVH in adulthood was associated with a trajectory of higher BP measurements beginning in childhood.[46] These observations reinforce the importance of measuring BP at regular intervals throughout childhood and adolescence.

Linking Hypertension to Cardiovascular Events in Adults

Increasing BP is on a continuum with increasing risk of adverse cardiovascular outcomes in old age: with each 20 mm Hg SBP or 10 mm Hg DBP rise above a threshold of 115/75 mm Hg, the risk of death from heart disease, stroke or other vascular disease is doubled.[47] Subgroup analysis within a recent meta-analysis of subjects aged <30 years showed that compared with "optimal BP" (BP < 120/80 mm Hg), the relative risk (RR) of any adverse cardiovascular event for Grade 1 hypertension (140–159/90–99 mm Hg) was 1.46 (1.24–1.72) and for Grade 2 hypertension was 2.22 (1.46–3.39).[48] These data support the current hypertension guidelines for young adults. For all participants 18 to 45 years, number needed to treat (NNT) for one year to prevent one cardiovascular event for those with Stage 2 hypertension was 236 and for high normal BP was 1450.[48]

Defining Hypertension in Children

BP increases physiologically throughout childhood with increasing age and height, with the largest increment during adolescence, and with greater changes in boys than girls. The diagnosis of hypertension in children has historically been based on normative values for age, height, and sex and defined as BP > 95th percentile.

- The 2017 AAP updated diagnostic criteria offered a simplified single threshold for children of ≥13 years of 130/80 mm Hg in line with the adult American Heart Association definition.[10]
- Hypertension Canada similarly in 2020 suggested a simplified threshold of 120/80 mm Hg for 6–11-year-olds and 130/85 mm Hg for ≥ 12-year-olds.[11]
- The 2016 ESH guideline specifies that the 95th centile should be used for hypertension diagnosis in all young people <16 years, and a threshold of 140/90 mm Hg in those ≥16 years to keep in line with adult ESH thresholds.[49]

Normative data for the 2016 ESH guidelines are taken from the "2004 Fourth Report." Of note, both European and Canadian datasets were derived from healthy US children from the NHANES program, but the 2017 AAP guidelines excluded overweight and obese children from this dataset. These differences between Clinical Practice Guidelines highlight the significant knowledge gaps that remain to help make firm and grounded recommendations to lower age cutoffs. The decision of what age to transition to an "adult" single cutoff remains difficult as it implies that age, sex, and height have become irrelevant.

Since the publication of the 2017 AAP and 2016 ESH guidelines, considerable research and debate has focused on which approach maximizes positive predictive value for patients at risk of cardiovascular morbidity.[50,51] Application of the 2017 AAP guidelines in longitudinal cohorts increases the prevalence of hypertension for most patients compared with the 2004 Fourth Report and 2016 ESH guidelines, especially for those with excess weight.[15,50] A recent systematic review and meta-analysis found that although the 2017 AAP guideline classified more patients as hypertensive, no difference in detection of LVH within hypertensive groups was seen.[52] Despite the differing guidelines, there is widespread consensus that both approaches are clinically valid in the absence of definitive data on cardiovascular endpoints, and that studies delineating the optimum BP threshold to lower the risk of these cardiovascular endpoints are urgently needed.[51] Overall, these issues also highlight that the relationships among age, body size, and left ventricular mass (LVM) are complex, especially during the process of growth as seen during adolescence.

Hypertension-Mediated Organ Damage

In the absence of longitudinal data linking childhood hypertension to cardiovascular events, the rationale for identifying and treating hypertension is largely based on evidence reporting markers of hypertensive-mediated organ damage (HMOD) in hypertensive young people.

Indexed left ventricular mass (LVMI) expressed as $g/m^{2.7}$ is the most widely reported HMOD marker, shown to relate to adverse cardiovascular outcomes in adults.[53] Increased prevalence of LVH has been consistently found in hypertensive compared with normotensive pediatric cohorts, but the percentile of BP above which the risk for LVH increases has been unclear.[54] A recent multicentre cohort study in the United States has improved clarity regarding this issue. Echocardiography in 360 participants stratified into low-, mid-, and high-risk BP (BP < 80th, 81st-90th, and >90th percentiles, respectively) found a stepwise increase in LVMI across BP risk groups.[55] LVH was present in 13%, 21%, and 27% of the low-, mid-, and high-risk groups, respectively.[55] Following specific analysis of increasing SBP, the 90^{th} percentile represented the best balance between sensitivity (0.44) and specificity (0.75) to predict presence of LVH, suggesting that evaluation for LVH may be indicated if clinic SBP >90th centile.[55]

In addition to cardiac remodeling, pediatric hypertension is associated with signs of early vascular aging, in the form of structural (as assessed by carotid intima medial thickness, cIMT) and functional (as assessed by carotid-femoral PWV, PWVcf, and flow-mediated dilatation) impairment of the arterial tree.[56] Urbina and colleagues[57] reported progressive worsening of arterial stiffness measures with increasing BP levels in a large cohort of hypertensive and normotensive adolescents. Neurocognitive impairment in those with PH has been suggested, implying involvement of the wider vascular tree.[58] Microvascular components of the arterial tree are also impacted as shown in a recent study reporting a close association between macrovascular injury (increased cIMT) and retinal microcirculation injury (increased foveal avascular zone).[59] At present, no guidelines recommend specific investigation for vascular HMOD outside the research setting due to insufficient normative data.

Importantly, evidence supporting the reversibility of LVH in children was reported by Litwin and colleagues with a reduction in LVH from 47% to 31% after 12 months of antihypertensive therapy. They reported a reduction in excess weight as an independent predictor for LVH regression.[33] This is corroborated by weight loss studies in obese young people; with one study finding that a combined diet and exercise weight reduction program is more effective at reducing cIMT than dietary interventions alone, although BP outcomes were not presented.[60] These data highlight the value of early

and aggressive management of hypertension in the presence of HMOD and the importance of a multifaceted approach to treatment including lifestyle modification.

Investigation and Diagnosis

Suggested pathway to diagnosis and management is covered in detail in the relevant guidelines, with evidence for rationale, and is summarized in **Fig. 2.**[10,11,49,61] Following confirmation of high office BP, the most helpful procedure is out-of-office BP measurement in the form of 24-h ambulatory BP measurement (ABPM). This is recommended to confirm the diagnosis of hypertension and has been found to be cost-effective in a hospital setting, as a normal ABPM study often negates the need for significant further investigation.[62]

Although ABPM is the gold standard, it is not feasible across all settings or patients. Purchase of ABPM equipment and training staff to use and interpret the results is expensive and difficult to implement in general pediatric settings, not to mention LIMCs. ABPM is not recommended in children under 5 due to lack of normative data and lack of feasibility, and may not be tolerated in some special populations of children over 5. In such cases, Home BP (HBP) monitoring can be a useful adjunct

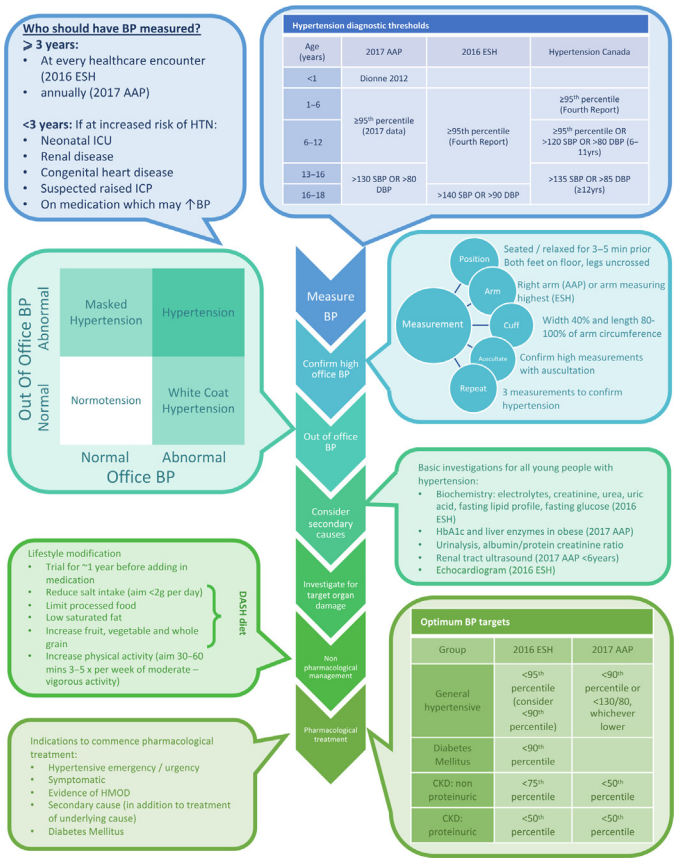

Fig. 2. Hypertension diagnosis and management: key factors. AAP, American Academy of Pediatrics guidelines 2017; BP, blood pressure; CKD, chronic kidney disease; DASH, dietary approaches to stop hypertension; DBP, diastolic BP; ESH, European Society for Hypertension guidelines 2016; HTN, hypertension; ICP, intracranial pressure; ICU, intensive care unit; SBP, systolic BP.

to gain some insight into out-of-office BP. HBP has been shown to correlate with ABPM, office BP and for SBP, signs of HMOD.[63] A validated oscillometric device can be used but these are known to overestimate BP in children. HBP monitoring using a doppler probe to detect SBP has also been shown to have a good correlation with office BP and to be feasible to teach to parents.[64] However, normative data for HBP monitoring with either automated or doppler devices do not currently exist and published experience remains limited outside single centers for HBP. Additional clinical studies are needed, although a recent systematic review on HBP concluded that until further data become available, a 7-day, morning, and evening (minimum 12) series of measurements should be used for HBP.[63]

Once the diagnosis of hypertension has been confirmed, a targeted consideration and investigation for secondary causes should be undertaken. Beyond a basic investigation panel indicated in every young person diagnosed with hypertension (see **Fig. 2**), this will vary according to the clinical situation. **Table 1** summarizes common secondary causes with investigations to consider.[65] An echocardiogram to assess for HMOD is recommended for all patients with hypertension by 2016 ESH guidelines and at the time of consideration of pharmacological therapy by 2017 AAP guidelines.[10,49]

Treatment

For PH and high normal BP in the absence of symptoms or markers of HMOD, the first-line management outlined in all major guidelines is lifestyle modification; primarily reduction in salt intake and weight loss through dietary modification and increased exercise. Focus on lifestyle modification should continue following initiation of medication, especially in the case of obesity-related hypertension where weight loss is the most important therapeutic intervention.[10,49]

A recent randomized controlled trial (RCT) showed that an intervention consisting of four 90-min exercise sessions per week for 1 year reduced the proportion of children in hypertensive BP range from 86% to 16% in a group of obese children with a mean age of 10.4 $\pm$ 1.4 years.[66] Meta-analyses of studies focusing on general and obese populations show more modest reductions of 1-2 mm Hg for both SBP and DBP from exercise programs involving three or more sessions lasting at least 60 minutes per week.[67]

Salt intake has long been associated with BP.[68,69] In adults, a decreased salt intake of 6 g/day was associated with a fall in SBP of approximately 6 mm Hg.[69] In children, a 42% reduction in salt intake was associated with a decrease in SBP of 2.47 mm Hg (4.00 to 0.94 mm Hg; $P < 0.01$).[68] There is evidence that salt intake from infancy influences BP trajectory. A 20-year follow-up of participants in a neonatal salt restriction study found a lower SBP of 3.6 mm Hg (-6.6 to -0.5) in those assigned a lower salt diet as a neonate.[70]

Given the prevalence of salt in processed foods, for families who find it difficult to reduce the proportion of processed foods in their diet, referral to a dietician or community/school-based dietary education program may be more effective than advice alone. One large 20-year prospective study found that following bi-annual dietary advice focused on increasing fruit, vegetables, and fiber and reducing saturated fat, attainment of these dietary targets was associated with a modest reduction in BP.[71] Interest has gathered around the Dietary Approaches to Stop Hypertension (DASH), a healthy eating approach specific to hypertension by promoting foods that are low in sodium, high in potassium and magnesium, and low in saturated fat. Evidence of its efficacy in children is limited mainly due to lack of data and poor adherence to the diet in the few RCTs which have been performed.[72]

Indications for commencing antihypertensive therapy and target BP are detailed in **Fig. 2**. There is very limited evidence to support which medication to use; the most

Table 1
Important secondary causes for hypertension with suggested diagnostic investigations

Category	Specific Cause	Investigations
All hypertension cases		Renal ultrasound scan Plasma electrolytes, creatinine, and urea Urinalysis Urine albumin: creatinine ratio Echocardiogram (2016 ESH)
Obesity		Fasting glucose &/or $HbA1_c$ Lipid profile Uric acid
	In selected cases only	
Parenchymal renal disease	Glomerulonephritis Focal and segmental glomerulosclerosis Pyelonephritis-related renal scarring Acute kidney injury with salt and water overload Polycystic kidney disease Chronic kidney disease Obstructive uropathy	Tc99 dimercaptosuccinic acid (DMSA) scan
Renovascular	Renal artery stenosis (*Idiopathic, Fibromuscular dysplasia, Neurofibromatosis type 1, Williams syndrome*) Mid-aortic syndrome Thrombosis of renal artery or vein Acute or post hemolytic uremic syndrome Fistulae External compression	Renin and aldosterone Doppler studies of renal arteries CT angiography MR angiogram Digital Subtraction Angiography (DSA) Selective renal vein renin measurement
Endocrine	Cortisol/glucocorticoid excess Aldosterone/mineralocorticoid excess Catecholamine excess Congenital adrenal hyperplasia Thyroid disease	Thyroid Function Tests Plasma cortisol Urinary steroid profile Plasma/urine catecholamines and metanephrines
Cardiovascular	Coarctation of aorta Takayasu arteritis	Echocardiogram Cardiac MRI
Central nervous system	Pain Convulsions Increased intracranial pressure Guillain–Barré syndrome Dysautonomia	
Malignancy	Wilms' tumor (nephroblastoma) Neuroblastoma Pheochromocytoma	Plasma/urine catecholamines and metanephrines Metaiodobenzylguanidine (MIBG) scan CT abdomen/pelvis

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Table 1
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Category	Specific Cause	Investigations
Drugs	Amphetamine or sympathomimetics Acute vitamin D intoxication, hypercalcemia Calcineurin inhibitors (ciclosporin/tacrolimus) Decongestants Erythropoietin Oral contraceptive pills Steroids	Urine toxicology screen
Others	Obstructive sleep apnea Bronchopulmonary dysplasia Single gene defects causing hypertension (eg, Liddle's syndrome)	Sleep study

Investigations are suggested for each category rather than specific causes and may not be indicated in all cases.

Adapted from Singh C, Jones H, Copeman H, Sinha MD. Fifteen-minute consultation: the child with systemic arterial hypertension. Arch Dis Child Educ Pract Ed. 2017 Feb;102(1):2-7.

recent meta-analysis in 2018 found angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) are superior to placebo.[73] A recent interesting study adopted an n-of-1 methodology (single patient randomized crossover trials) to develop a personalized approach to antihypertensive medication choice.[74] Lisinopril was preferred and effective in 16 of the 32 patients studied, with the next most popular agents being amlodipine and hydrochorothiazide.[74]

Until further data become available, ACEi, ARB, calcium channel blocker, or thiazide diuretic could be considered as initial agents, starting at the lowest dose and titrating up every 2-4 weeks until BP is in the target range.[10,49] ACEi/ARB are most suitable as they increase insulin sensitivity and peripheral blood flow but have potential side effects and need to be avoided in sexually active girls. Calcium channel blockers are useful first-line agents but may be associated with pedal edema. Beta-blockers especially more recent agents in those with evidence of hyperdynamic circulation are helpful and all agents can be used in combination. There may be specific circumstances in which choice of medication is clear, eg, ACEi/ARB in chronic kidney disease with proteinuria, a diuretic in corticosteroid-induced hypertension. If a second agent is needed, a thiazide diuretic is useful to counter the salt and water retention caused by several other medications.

Challenges in Management

Hypertension in children and young adults is an expanding clinical problem. However many clinical settings are not resourced to measure or interpret BP and there remains heterogeneity in its management which is discordant with the published guidelines. Further, hypertension is poorly screened for and recognized, especially in obese young people.[75] Diagnosis depends on out-of-office BP monitoring, a limited resource to clinicians in primary and secondary care, and in LIMCs.[76] Diet, weight control, and increased physical activity are the most important management strategy for obesity-related hypertension and yet parity of access to multidisciplinary weight loss services is not clear. Engagement with lifestyle modification interventions is notoriously

Fig. 3. Transition to adult services–suggested schematic of key themes. (Based on Nagra A, McGinnity PM, Davis N, Salmon AP. Implementing transition: Ready Steady Go. Arch Dis Child Educ Pract Ed. 2015 Dec;100(6):313-20 [www.readysteadygo.net] and National Institute for Health and Care Excellence, Transition from children's to adults' services. Quality standard [QS140] Published date: 21 December 2016.)

difficult, especially as most PH patients are adolescents, a group of patients with specific needs and vulnerabilities.

Transition to Adult Services

Adolescence and transition to adult services is a particularly challenging period of clinical care for young people, their families, and clinical teams. Young people are expected to follow a developmental trajectory that culminates in self-management of their condition, but the speed and pattern of this trajectory may not align with the traditional timings of transition from pediatric to adult care.[77] In hypertension this is even more problematic; as a largely asymptomatic condition, there are high risks for young people to drop out of clinical care and/or medication compliance.[78] Children with PH are often cared for by pediatric specialists (eg, nephrologists or cardiologists) however adult hypertension care may be based on cardiology or family medicine/general practice depending on local arrangements and the severity of the condition. This adds to the complexity of the transition process and to the opportunity for interruptions in care. Regardless of the quality of BP control under pediatric care, if a young adult drops out of care during the transition to adult services, there may be significant effects on their cardiovascular risk.[48] There are no unified guidelines to aid in the planning of transition services for young people with hypertension but suggested general good practice principles are outlined in **Fig. 3**.[79,80]

SUMMARY

Hypertension in children and young adults is a growing clinical problem linked to the increasing prevalence of obesity worldwide. If BP is poorly controlled, there is likely to be a significant increase in health care-related costs due to excess adverse cardiovascular events in middle age or sooner. Improvements in care for this group of patients depend on prompt diagnosis, supported nonpharmacological interventions, and robust local frameworks for the transition from pediatric to adult services. Future research should aim to address unknowns regarding future risk of adverse cardiovascular outcomes, establish normative datasets for home BP monitoring and elucidate the hemodynamic processes distinguishing hypertension in young people. These may form the starting point for randomized controlled trials into optimum antihypertensive agents for different hypertensive phenotypes, patient ethnicities, and underlying etiologies.

CLINICS CARE POINTS

- Clinicians should have an increasing index of suspicion for primary rather than secondary hypertension with increasing age and especially in the context of excess weight."
- There is currently no role for genetic testing in paediatric hypertension unless a monogenic cause is suspected.
- Out of office BP monitoring should be used to support a diagnosis of hypertension and investigate for white coat hypertension. ABPM is preferred."
- Guidelines differ regarding diagnostic threshold, minimum investigations and treatment threshold for managing hypertension."
- Lifestyle changes remain the most important management strategy for primary hypertension and include a combination of weight management, reduction in salt intake and moderate exercise."

DISCLOSURE

The authors have nothing to disclose.

REFERENCES

1. Hypertension: fact sheet, world health organisation. Available at: https://www.who.int/health-topics/hypertension#tab=tab_1. Accessed 10th January, 2022.
2. Gupta-Malhotra M, Banker A, Shete S, et al. Essential hypertension vs. secondary hypertension among children. Am J Hypertens 2015;28(1):73–80.
3. Khoury M, Urbina EM. Hypertension in adolescents: diagnosis, treatment, and implications. Lancet Child Adolesc Health 2021;5(5):357–66.
4. Dionne JM. Evidence gaps in the identification and treatment of hypertension in children. Can J Cardiol 2020;36(9):1384–93.
5. Taylor-Zapata P, Baker-Smith CM, Burckart G, et al. Research gaps in primary pediatric hypertension. Pediatrics 2019;143(5).
6. Song P, Zhang Y, Yu J, et al. Global Prevalence of Hypertension in Children: A Systematic Review and Meta-analysis. JAMA Pediatr 2019;173(12):1154–63.
7. Sun J, Steffen LM, Ma C, et al. Definition of pediatric hypertension: are blood pressure measurements on three separate occasions necessary? Hypertens Res 2017;40(5):496–503.

8. Chiolero A, Cachat F, Burnier M, et al. Prevalence of hypertension in schoolchildren based on repeated measurements and association with overweight. J Hypertens 2007;25(11):2209–17.
9. Nsanya MK, Ayieko P, Hashim R, et al. Sustained high blood pressure and 24-h ambulatory blood pressure monitoring in Tanzanian adolescents. Sci Rep 2021; 11(1):8397.
10. 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.
11. Rabi DM, McBrien KA, Sapir-Pichhadze R, et al. Hypertension Canada's 2020 comprehensive guidelines for the prevention, diagnosis, risk assessment, and treatment of hypertension in adults and children. Can J Cardiol 2020;36(5): 596–624.
12. Larkins NG, Teixeira-Pinto A, Kim S, et al. The population-based prevalence of hypertension and correlates of blood pressure among Australian children. Pediatr Nephrol 2019;34(6):1107–15.
13. Robinson SK, Rodd CJ, Metzger DL, et al. Prevalence of high blood pressure among Canadian Children: 2017 American Academy of Pediatrics guidelines with the Canadian Health Measures Survey. Paediatr Child Health 2021;26(3): e158–65.
14. Martin L, Oepen J, Reinehr T, et al. Ethnicity and cardiovascular risk factors: evaluation of 40,921 normal-weight, overweight or obese children and adolescents living in Central Europe. Int J Obes (Lond) 2015;39(1):45–51.
15. Sharma AK, Metzger DL, Rodd CJ. Prevalence and severity of high blood pressure among children based on the 2017 american academy of pediatrics guidelines. JAMA Pediatr 2018;172(6):557–65.
16. Lurbe E, Torró I, Álvarez J, et al. Impact of ESH and AAP hypertension guidelines for children and adolescents on office and ambulatory blood pressure-based classifications. J Hypertens 2019;37(12):2414–21.
17. Sarki AM, Nduka CU, Stranges S, et al. Prevalence of hypertension in low- and middle-income countries: a systematic review and meta-analysis. Medicine (Baltimore) 2015;94(50):e1959.
18. Ajayi IO, Soyannwo MAO, Asinobi AO, et al. Blood pressure pattern and hypertension related risk factors in an urban community in Southwest Nigeria: The Mokola hypertension initiative project, Ibadan, Nigeria. J Public Health Epidemiol 2017;9:51–64.
19. Verma M, Chhatwal J, George SM. Obesity and hypertension in children. Indian Pediatr 1994;31(9):1065–9.
20. Katamba G, Agaba DC, Migisha R, et al. Prevalence of hypertension in relation to anthropometric indices among secondary adolescents in Mbarara, Southwestern Uganda. Ital J Pediatr 2020;46(1):76.
21. Chelo D, Mah EM, Chiabi EN, et al. Prevalence and factors associated with hypertension in primary school children, in the centre region of Cameroon. Transl Pediatr 2019;8(5):391–7.
22. Aggarwal A, Rodriguez-Buritica D. Monogenic hypertension in children: a review with emphasis on genetics. Adv Chronic Kidney Dis 2017;24(6):372–9.
23. Wang X, Xu X, Su S, et al. Familial aggregation and childhood blood pressure. Curr Hypertens Rep 2015;17(1):509.
24. Huang Y, Ollikainen M, Muniandy M, et al. Identification, heritability, and relation with gene expression of novel DNA methylation loci for blood pressure. Hypertension 2020;76(1):195–205.

25. Surendran P, Feofanova EV, Lahrouchi N, et al. Discovery of rare variants associated with blood pressure regulation through meta-analysis of 1.3 million individuals. Nat Genet 2020;52(12):1314–32.
26. Ehret GB, Munroe PB, Rice KM, et al. Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk. Nature 2011;478(7367):103–9.
27. Cecelja M, Keehn L, Ye L, et al. Genetic aetiology of blood pressure relates to aortic stiffness with bi-directional causality: evidence from heritability, blood pressure polymorphisms, and Mendelian randomization. Eur Heart J 2020;41(35):3314–22.
28. Litwin M, Kułaga Z. Obesity, metabolic syndrome, and primary hypertension. Pediatr Nephrol 2021;36(4):825–37.
29. Maximova K, O'Loughlin J, Paradis G, et al. Changes in anthropometric characteristics and blood pressure during adolescence. Epidemiology 2010;21(3):324–31.
30. Sorof JM, Poffenbarger T, Franco K, et al. Isolated systolic hypertension, obesity, and hyperkinetic hemodynamic states in children. J Pediatr 2002;140(6):660–6.
31. Naidoo S, Kagura J, Fabian J, et al. Early Life factors and longitudinal blood pressure trajectories are associated with elevated blood pressure in early adulthood. Hypertension 2019;73(2):301–9.
32. Freedman DS, Goodman A, Contreras OA, et al. Secular trends in BMI and blood pressure among children and adolescents: the Bogalusa Heart Study. Pediatrics 2012;130(1):e159–66.
33. Litwin M, Niemirska A, Sladowska-Kozlowska J, et al. Regression of target organ damage in children and adolescents with primary hypertension. Pediatr Nephrol 2010;25(12):2489–99.
34. Brady TM. Obesity-Related Hypertension in Children. Front Pediatr 2017;5:197.
35. Franklin SS, Jacobs MJ, Wong ND, et al. Predominance of isolated systolic hypertension among middle-aged and elderly US hypertensives: analysis based on National Health and Nutrition Examination Survey (NHANES) III. Hypertension 2001;37(3):869–74.
36. Alsaeed H, Metzger DL, Blydt-Hansen TD, et al. Isolated diastolic high blood pressure: a distinct clinical phenotype in US children. Pediatr Res 2021;90(4):903–9.
37. McEniery CM, Yasmin, Wallace S, et al. Increased stroke volume and aortic stiffness contribute to isolated systolic hypertension in young adults. Hypertension 2005;46(1):221–6.
38. Gu H, Singh C, Li Y, et al. Early ventricular contraction in children with primary hypertension relates to left ventricular mass. J Hypertens 2021;39(4):711–7.
39. Nardin C, Maki-Petaja KM, Miles KL, et al. Cardiovascular phenotype of elevated blood pressure differs markedly between young males and females: the enigma study. Hypertension 2018;72(6):1277–84.
40. Falkner B. Cardiac output versus total peripheral resistance. Hypertension 2018;72(5):1093–4.
41. Li Y, Haseler E, Chowienczyk P, et al. Haemodynamics of hypertension in children. Curr Hypertens Rep 2020;22(8):60.
42. Litwin M, Feber J. Origins of primary hypertension in children. Hypertension 2020;76(5):1400–9.
43. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. Circulation 2008;117(25):3171–80.

44. Sinha MD. From pregnancy to childhood and adulthood: the trajectory of hypertension. In: Lurbe EW E, editor. Hypertension in children and adolescents: new perspectives. Switzerland AG: Springer Nature; 2019. p. 1–16, chap 1. Updates in Hypertension and Cardiovascular Protection.
45. Urbina EM, Khoury PR, Bazzano L, et al. Relation of blood pressure in childhood to self-reported hypertension in adulthood. Hypertension 2019;73(6):1224–30.
46. Zhang T, Li S, Bazzano L, et al. Trajectories of childhood blood pressure and adult left ventricular hypertrophy: the bogalusa heart study. Hypertension 2018; 72(1):93–101.
47. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002;360(9349):1903–13.
48. Luo D, Cheng Y, Zhang H, et al. Association between high blood pressure and long term cardiovascular events in young adults: systematic review and meta-analysis. BMJ 2020;370:m3222.
49. Lurbe E, Agabiti-Rosei E, Cruickshank JK, et al. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. J Hypertens 2016;34(10):1887–920.
50. Khoury M, Khoury PR, Dolan LM, et al. Clinical Implications of the Revised AAP Pediatric Hypertension Guidelines. Pediatrics 2018;142(2):e20180245.
51. Stabouli S, Redon J, Lurbe E. Redefining hypertension in children and adolescents: a review of the evidence considered by the European Society of Hypertension and American Academy of Pediatrics guidelines. J Hypertens 2020;38(2): 196–200.
52. Di Bonito P, Valerio G, Pacifico L, et al. Impact of the 2017 Blood Pressure Guidelines by the American Academy of Pediatrics in overweight/obese youth. J Hypertens 2019;37(4):732–8.
53. Levy D, Garrison RJ, Savage DD, et al. Prognostic implications of echocardiographically determined left ventricular mass in the framingham heart study. New Engl J Med 1990;322(22):1561–6.
54. Woroniecki RP, Kahnauth A, Panesar LE, et al. Left ventricular hypertrophy in pediatric hypertension: a mini review. Front Pediatr 2017;5:101.
55. Urbina EM, Mendizábal B, Becker RC, et al. Association of blood pressure level with left ventricular mass in adolescents. Hypertension 2019;74(3):590–6.
56. Litwin M, Feber J. Origins of primary hypertension in children: early vascular or biological aging? Hypertension 2020;76(5):1400–9.
57. Urbina EM, Khoury PR, McCoy C, et al. Cardiac and vascular consequences of pre-hypertension in youth. J Clin Hypertens (Greenwich) 2011;13(5):332–42.
58. Lande MB, Batisky DL, Kupferman JC, et al. Neurocognitive function in children with primary hypertension. J Pediatr 2017;180:148–55.e1.
59. Rogowska A, Obrycki Ł, Kułaga Z, et al. Remodeling of retinal microcirculation is associated with subclinical arterial injury in hypertensive children. Hypertension 2021;77(4):1203–11.
60. Woo KS, Chook P, Yu CW, et al. Effects of diet and exercise on obesity-related vascular dysfunction in children. Circulation 2004;109(16):1981–6.
61. Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: diagnosis, management and outcome. Pediatr Nephrol 2012;27(1):17–32.
62. Swartz SJ, Srivaths PR, Croix B, et al. Cost-effectiveness of ambulatory blood pressure monitoring in the initial evaluation of hypertension in children. Pediatrics 2008;122(6):1177–81.

63. Stergiou G, Stambolliu E, Bountzona I, et al. Home blood pressure monitoring in children and adolescents: systematic review of evidence on clinical utility. Curr Hypertens Rep 2019;21(8):64.
64. Newton J, Singh C, Sinha MD. Measurement of SBP at home by parents using hand-held Doppler device and aneroid sphygmomanometer: a single-centre experience. J Hypertens 2021;39(5):904–10.
65. Singh C, Jones H, Copeman H, et al. Fifteen-minute consultation: the child with systemic arterial hypertension. Arch Dis Child Educ Pract Ed 2017;102(1):2–7.
66. Aguilar-Cordero MJ, Rodríguez-Blanque R, Leon-Ríos X, et al. Influence of physical activity on blood pressure in children with overweight/obesity: a randomized clinical trial. Am J Hypertens 2020;33(2):131–6.
67. Cai L, Wu Y, Wilson RF, et al. Effect of childhood obesity prevention programs on blood pressure: a systematic review and meta-analysis. Circulation 2014;129(18):1832–9.
68. He FJ, MacGregor GA. Importance of salt in determining blood pressure in children: meta-analysis of controlled trials. Hypertension 2006;48(5):861–9.
69. He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: cochrane systematic review and meta-analysis of randomised trials. BMJ 2013;346:f1325.
70. Geleijnse JM, Hofman A, Witteman JC, et al. Long-term effects of neonatal sodium restriction on blood pressure. Hypertension 1997;29(4):913–7.
71. Laitinen TT, Nuotio J, Niinikoski H, et al. Attainment of targets of the 20-year infancy-onset dietary intervention and blood pressure across childhood and young adulthood. Hypertension 2020;76(5):1572–9.
72. Paula Bricarello L, Poltronieri F, Fernandes R, et al. Effects of the Dietary Approach to Stop Hypertension (DASH) diet on blood pressure, overweight and obesity in adolescents: a systematic review. Clin Nutr ESPEN 2018;28:1–11.
73. Burrello J, Erhardt EM, Saint-Hilary G, et al. Pharmacological treatment of arterial hypertension in children and adolescents: a network meta-analysis. Hypertension 2018;72(2):306–13.
74. Samuel JP, Tyson JE, Green C, et al. Treating hypertension in children with n-of-1 trials. Pediatrics 2019;143(4):e20181818.
75. Rea CJ, Brady TM, Bundy DG, et al. Pediatrician adherence to guidelines for diagnosis and management of high blood pressure. J Pediatr 2021;242(e1):12–7.
76. Peterson CG, Miyashita Y. The use of ambulatory blood pressure monitoring as standard of care in pediatrics. Front Pediatr 2017;5:153.
77. Farre A, McDonagh JE. Helping health services to meet the needs of young people with chronic conditions: towards a developmental model for transition. Healthcare (Basel) 2017;5(4):77.
78. Chung RJ, Mackie AS, Baker A, et al. Cardiovascular risk and cardiovascular health behaviours in the transition from childhood to adulthood. Can J Cardiol 2020;36(9):1448–57.
79. Nagra A, McGinnity PM, Davis N, et al. Implementing transition: ready Steady Go. Arch Dis Child Educ Pract Ed 2015;100(6):313–20.
80. National Institute for Health and Care Excellence. Transition from children's to adults' services, quality standard [QS140] 2016.