European Society of Hypertension Scientific Newsletter:
Update on Hypertension Management

2002; 3: No. 13

HYPERTENSION IN CHILDREN AND ADOLESCENTS

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Definition of Hypertension

Of all that is known about the levels and distribution of casual blood pressure (BP) in childhood and adolescents, two facts are well accepted: blood pressure increases during growth and maturation, and adolescence is a fast growth period during which body mass and BP change rapidly. These are the main reasons for why reference BP values over the last few decades have been referred to as ones specific to sex, age, and/or height in children and adolescents up to 18 years of age.

Using the Task Force data table (1), normal BP is defined as systolic and diastolic BP less than the 90th percentile for age, sex and height. Borderline, or high normal BP, is defined as an average systolic and/or average diastolic BP between the 90th and 95th percentiles for age, sex and height. Hypertension is defined as an average systolic and/or average diastolic BP greater than or equal to the 95th percentile for age, sex and height, measured on at least 3 separate occasions.

Statistically, 5% of children had a BP measurement higher than the 95th percentile during a single office visit. Blood pressure however, tended to normalize on subsequent measurements due to the accommodation of the child to the measurement procedure and to the statistical phenomenon of regression toward the mean. Consequently, the prevalence of hypertension decreased to 1% after only one repeated examination. (The diagnostic algorithm of hypertension is found in Figure 1). Elevated BP in childhood may be detected during the evaluation of a child with chronic illness or in subpopulations of children at increased risk for hypertension. The objective of detecting high BP in children is to identify those who are at risk for the morbidity and mortality associated with hypertension. The detection of childhood hypertension is important because hypertension is frequently related to an identifiable and potentially treatable disease process, while untreated severe hypertension in childhood is associated with significant morbidity and mortality (2).

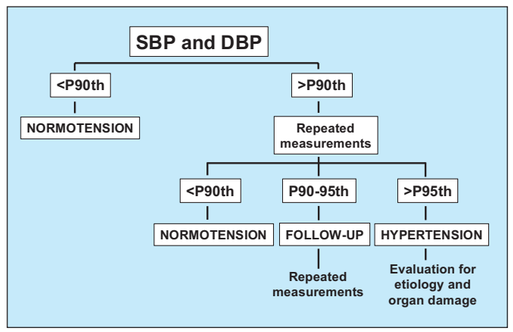

Figure 1. Algorithm diagnostic of hypertension in children and adolescents.

Although it is generally agreed that early essential hypertension poses little immediate risk to most children, it carries the potential for future end-organ damage. In children, accurate identification of hypertension at the earliest possible age would, therefore, give health-care providers the opportunity to initiate preventive measures, thereby reducing the chance of developing end-organ damage and its attendant morbidity and mortality. Consequently, repeated BP measurements over time would become a routine part of pediatric well-child care.

Etiology of Childhood Hypertension

Usually, sustained hypertension in children and adolescents is classified as secondary with a specific cause that may be correctable or as essential and without an identifiable cause. The most common causes of hypertension can change during childhood. Essential hypertension is rarely seen in infants and young children, but its prevalence increases significantly in adolescence. A good general rule to follow is that the likelihood of identifying a secondary cause of hypertension is inversely related to the age of the child and directly related to the degree of BP elevation. The evaluation of children with hypertension, especially young children and those with severe hypertension, should be comprehensive and aimed at identifying known causes of the disease.

Table 1. Most Common Causes of Hypertension by Age Group

< 1 Month	**> 6 Years to 10 Years**
● Renal arterial thrombosis ● Coarctation of the aorta ● Congenital renal disease ● Bronchopulmonary dysplasia	● Renal parenchymal disease ● Renovascular disease ● Essential hypertension
>1 Month to <6 Years	**> 10 Years to 18 Years**
● Renal parenchymal disease ● Coarctation of the aorta ● Renovascular disease	● Essential hypertension ● Renal parenchymal disease ● Renovascular disease

Definable causes of hypertension are associated with a broad spectrum of diseases. The distribution of causes clearly varies with age. A rational approach based on a careful clinical evaluation and simple algorithms permits a direct evaluation, saving time and avoiding unnecessary tests. Since the definable causes of hypertension vary according to age, the approach to diagnosis may differ slightly at different ages.

Renal parenchymal disorders with renovascular disease, and coarctation of the aorta account for 70% to 90% (3) of all cases. These figures vary depending not only on the age group, but also on referral center and referral bias. Additionally, hypertension is often related to prescribed drugs with hypertensive potential. Other infrequent causes of sustained hypertension, tumors and central nervous and endocrine disorders, must be considered once more common causes of secondary hypertension have been eliminated.
Hypertension in term or preterm neonates may be seen in up to 2% of all infants in modern neonatal intensive care units. As in older children, the causes of hypertension in neonates are numerous, with the two largest categories being renovascular and parenchymal diseases. More specifically, umbilical artery catheter-associated thromboembolism affecting either the aorta and/or the renal arteries probably accounts for the majority of cases of hypertension seen in the typical neonatal intensive care unit (4).

In very young children (<6 years), hypertension is most often the result of such renal parenchymal disease as glomerulonephritis, renal scarring, polycystic kidney diseases, and renal dysplasia. Renal artery stenosis and cardiovascular disorders like coarctation of the aorta, less frequent causes of hypertension in this age group, are usually detected within the first decade of life.

Late in the first decade and throughout the second, essential hypertension becomes the most common cause of sustained hypertension, particularly in those children with mild asymptomatic disease. In this age group, a predominance of isolated systolic hypertension is observed. The pathophysiology of essential hypertension is not well understood and likely involves not only genetic predisposition, but also environmental, lifestyle and fetal factors.

The majority of individuals with essential hypertension have complex polygenic abnormalities combined with predisposing environmental factors. A genetic influence clearly exists; familial BP patterns have been well established and are recognized as early as infancy. Family studies have demonstrated that at least 20% to 40% of the BP variance in the population can be ascribed to familial factors (5).

Substantial clinical and epidemiological evidence supports the influence of obesity in BP levels even early in life. Obesity acquired during childhood, to some extent tracks into adult life, and since the relationship between obesity and hypertension is well established in adults, obese children appear to be at particularly high risk of becoming hypertensive adults (6).

There has recently been an increasing interest in the influence of intrauterine life as a pathogenesis in the development of chronic diseases. Evidence comes from epidemiological studies which relate birth measurements, as a proxy for fetal nutrition, with levels of cardiovascular mortality and risk factors (7). Birth weight, a crude measure of fetal growth, includes length, fatness and head size. An inverse relationship between birth weight and BP levels has been demonstrated. Intrauterine growth retardation and relatively low birth weights, even within the normal range, are considered a risk factor in the development of essential hypertension (8). The factors linking fetal growth to BP values later in life remain elusive.

Among those subjects without identifiable causes of HTN and strong familial history, emerging cause of secondary hypertension are single gene mutations that produces large changes in BP (9). While these disorders are thought to be rare, their precise prevalence is unknown and their specific diagnosis requires a high level of clinical suspicion. A major focus of such studies has been the epithelial sodium channel, which can be activated by mutations in the channel subunits or mineralocorticoid receptor, and changes in the response to or production of mineralocorticoids. As a result, there are now clearly defined mendelian syndromes in which epithelial sodium channel activity is dysregulated, with the subsequent development of systemic hypertension with supressed plasma renin activity that can be attributed to a primary renal mechanism. There are several monogenic forms of human hypertension, including Liddle syndrome, glucocorticoid-remediable aldosteronism, mineralocorticoid apparent excess, Gordon syndrome and mineralocorticoid receptor hypersensitivity syndrome.

Treatment

The goal of treatment for children with hypertension is aimed to reduce BP to a level below the 95th percentile. There is little controversy about initiating antihypertensive therapy in patients with secondary forms of hypertension because of the usual chronicity of the problem and the documented beneficial effects. When the decision has been made to begin antihypertensive therapy, an individualized stepped-care approach is advocated for children, preferably with treatment that is specific to the etiology.

Weight loss in the obese child, increased physical activity, and dietary modifications of sodium and potassium intake can reduce BP in hypertensive children, particularly overweight adolescents with essential hypertension (10). Children and adolescents for whom nonpharmacologic therapies, have failed, have severe sustained hypertension or have established target organ damage, the addition of drug therapy to the nonpharmacologic regimen should be strongly considered.
There is a greater reluctance to begin treatment in a child with mild hypertension. Do healthy asymptomatic children who are identified as hypertensive on routine examination, but who have no underlying recognizable disease, have an increased cardiovascular risk? Should these patients be treated early, based on BP value alone? The consequences of hypertension detected in childhood and adolescence remain largely unknown because no long-term outcome data are available to relate childhood hypertension to increased cardiovascular risk in adulthood. Some evidence indicates, however, that childhood BP levels are related to BP later in life, and high BP levels are one of the main risk factors leading to adult cardiovascular disease. Assessment of early end-organ damage, such as left ventricular hypertrophy, present in some essential hypertensives in this age group (11), may give us a reason to start pharmacological treatment. Scientific information about the natural history of BP in the transition from childhood to adulthood and about the long-term effects of the therapy are necessary.

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