Arterial hypertension in childhood

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Abstract

Objective: To critically review recent medical literature, focusing on practical features that are relevant for diagnosis and outpatient treatment of pediatric hypertension.

Sources: Classic articles and systematic review of recent literature through electronic search of Medline and Lilacs databases over the last 10 years, using the key words arterial hypertension, newborns, infants, preschool, children and adolescents. Those articles containing relevant information were selected.

Summary of the findings: Arterial hypertension and obesity are public health problems all over the world. Essential arterial hypertension in adults begins in childhood and can also be secondary to several diseases. Pediatricians must measure the arterial pressure of the patients in a proper manner. When arterial hypertension is detected, it must be investigated in order to be adequately treated. The investigation depends on the age and the rising degree of the arterial pressure, taking into consideration the cause of hypertension, as well as its effects on target organs.

Conclusions: The early recognition of an abnormal arterial pressure followed by adequate investigation and treatment are required to reduce the cardiovascular and renal morbidity/mortality.


Introduction

Hypertension is a multifactorial clinical entity defined by the III Consenso Brasileiro de Hipertensão Arterial 1 (III Brazilian Consensus on Hypertension) as a syndrome characterized by elevated blood pressure associated with metabolic and hormonal changes and trophic phenomena (cardiac and vascular hypertrophy).

Essential hypertension is the most prevalent chronic disease in the world. Data collected from 1988 to 1991 by the Third National Health and Nutrition Examination Survey revealed that 24% of the non-institutionalized American population, that is, about 43 million people, have hypertension. 2 In Brazil, 15 to 20% of the adult population has hypertension. 3

Moreover, hypertension is a serious independent risk factor for cardiovascular disease, cerebral vascular accident (CVA) and renal disease. In the United States, acute myocardial infarction and cerebral vascular accident are the first and third causes of death, with a huge...
finance loss of over 259 billion dollars in direct and indirect costs. Ischemic coronary syndromes and CVA account for one third of the deaths in Brazil, and are also serious causes of workplace absenteeism and early retirement. Hypertension is, thus, a public health problem all over the world.

Fortunately, studies conducted with hypertensive adults show that an effective treatment of hypertension significantly reduces the risk of complications.

Pediatricians started paying due attention to hypertension in children and adolescents just 25 years ago. The addition of blood pressure measurements to routine physical examinations of children and the publication of norms for the evaluation of hypertension in childhood have revealed cases of previously undetected asymptomatic secondary hypertension, as well as of discrete elevation of blood pressure.

Presently it is already known that hypertension detected in some children may be secondary to, for example, renal disease, but may also indicate early onset of essential hypertension found in some adults.

This study reviews the technique for blood pressure measurement and the normal values of blood pressure in children and adolescents, and describes the strategies to investigate and treat hypertension in pediatric patients.

Normal blood pressure in children

One of the most important parameters in the studies of hypertension in children is the definition of reference values to be adopted.

For the adult population, the definition of hypertension is epidemiological, and the cutoff point is determined according to the population at risk of developing morbid events. Adult blood pressure is abnormal when it is above a certain level and is associated with coronary disease, CVA or renal disease. In these cases, the patient should be treated with drugs. For children and adolescents, however, the definition is statistical because no studies so far have determined what blood pressure levels are associated with future disease.

In the last few decades, the references usually followed in clinical practice have been those reported by an American board of experts, the Task Force. The Task Force Reports are recommended by the National Heart, Lung and Blood Institute and by the American Academy of Pediatrics. Their first report, published in 1977, was a set of tables and graphs based on a meta-analysis of three American studies, totaling 5789 children. In the second report, in 1987, references were drawn from data collected from studies with over 70 thousand children (white, black and Hispanics). In 1993, Rosner et al. published new tables with normality limits (90 and 95 percentiles) for each age group, sex, and height percentile, and were, thus, able to correct an important factor of error in the reference values - the size of the child. They drew data from eight American studies of the 1987 Task Force and from the Minnesota study.

In 1996, the most recent update of the 1987 Task Force Report was published. It adopted the concepts established by Rosner et al., with specific reference values for each height percentile, separated by age and sex.

A parameter for measurement of diastolic pressure was another change introduced in that update. The Korotkoff sound that defines diastolic pressure in children is controversial. In childhood and, particularly, in adolescence, differences of some millimeters of mercury (mmHg) are frequent between the fourth and fifth Korotkoff sounds. In some children, the sounds are heard down to zero mmHg. The 1996 update recommended the use of the fifth Korotkoff sound to define diastolic pressure, and thus set a uniform value for determination in all age groups.

Measurement of blood pressure

The Second American Task Force (1987) recommended that all children older than three years should have their blood pressure measured according to appropriate norms during outpatient pediatric follow-up visits. However, it is important to point out that, even below that age, children and infants should undergo routine blood pressure measurements. This is the only way to make an early diagnosis - before there is target organ damage - of potentially serious conditions, such as renovascular disease.

Blood pressure should be measured when the child is calm and quiet, in an agreeable environment, after 5 to 10 minutes of rest. The child should be sitting, and the right arm positioned at the heart level. The cuff should be wrapped firmly 2 to 3 cm above the antecubital fossa, and the rubber bladder should be positioned over the brachial artery. The width of the rubber bladder in the cuff should correspond to 40% of the arm circumference, and its length should cover 80 to 100% of the upper arm (Figure 1). There are only three cuff sizes for children and one for adolescents, and proper fit is thus one of the main causes of error in the measurement of blood pressure in children. If no cuff has the right size, the largest should be chosen, because a larger cuff does not usually mask true hypertension, while a smaller one may lead to even higher readings. The stethoscope should then be placed over the brachial artery. The cuff is inflated to 30 mmHg above the point where the radial pulse disappears, and deflated slowly, 2 to 3 mmHg per second. The first Korotkoff sound (appearance of sounds) has been set as the standard for systolic pressure, and the fifth sound (disappearance of sounds), for diastolic pressure.

Automatic methods are accepted in pediatric blood pressure measurements, particularly for newborns and infants, when auscultation is difficult, or when more frequent measurements are necessary, such as in intensive care.
However, these indirect methods are not fully reliable to determine the diastolic pressure, and have to be calibrated frequently. For these reasons, the auscultatory method is recommended for the measurement of blood pressure in children. Several measurements (at least two) should be made in different occasions to classify blood pressure in children and adolescents.6

 Blood pressure levels should be compared with the reference values adopted. The blood pressure tables in the 1996 Update on the 1987 Task Force should be used. These tables define blood pressure levels according to sex, age and height percentile. Blood pressure should be classified according to the following criteria:

– normal pressure: systolic and diastolic pressure below the 90 percentile;
– high-normal or borderline pressure: systolic or diastolic pressure between the 90 and 95 percentiles;
– hypertension: systolic or diastolic pressure above the 95 percentile, measured in three different occasions;
– white-coat hypertension: hypertension observed in the office but not confirmed by measurements during ambulatory blood pressure monitoring (ABPM).

ABPM has been widely used in the diagnosis of hypertension in adults, but there is significantly less experience with this method for children. It is based on the principle that repeated blood pressure measurements in 24 hours provide a better approximation of the true blood pressure level than one single measurement. Success rate for ABPM in children is high, from 70 to 80%, and is affected by age - older children and adolescents accept the examination better than younger children. In clinical practice, ABPM has been used more often to diagnose white-coat hypertension (children whose blood pressure is normal, but who become stressed and hypertensive in the presence of the physician) and in patients with borderline and unstable hypertension. It has also been useful in the assessment of the effects if anti-hypertensive drugs when it is not clear whether blood pressure is under total control, and in the diagnosis of circadian rhythm changes (when there is no nocturnal decline in blood pressure), which is an early sign of vascular reactivity disorders.1,7,12

It is important to point out that there is no evidence that this method should be used in routine evaluations of hypertensive patients. It does not replace, therefore, the clinical evaluation and the measurement of blood pressure in the office.1

Prevalence

Although predominant in adults, hypertension in children and adolescents is not a minor problem. Its prevalence rate varies widely, from 1 to 13%, in studies conducted by several Brazilian and foreign authors. Such variation reflects, mainly, the methodology adopted: normality criteria, age, number of visits, number of measurements per visit, and length of follow-up. The highest prevalence rates are found in studies that drew data from one single visit.13

When blood pressure is measured several times, as recommended for the diagnosis of hypertension, the prevalence rate tends to fall as a result of the regression-to-the-mean phenomenon, and because the child becomes used to the measurement procedure and calms down. The actual prevalence rate of hypertension in childhood thus falls significantly, to about 1%.14

Blood pressure in childhood as a risk factor for hypertension in the adult.

Epidemiological studies of hypertension in childhood have been an important source of data, and have provided consistent signs that systemic hypertension in the adult begins in childhood. Several longitudinal studies have demonstrated that the child with elevated blood pressure levels, even when within the normal limits, tends to show a progression along life, with higher levels than other individuals and greater chances of becoming an adult with hypertension. Of these longitudinal studies, those conducted by Bogalusa,15 and Muscatine16 are some of those worth mentioning. Their studies reported a strong correlation between hypertension and elevated weight/height indices; that is, hypertension in those cases was associated with overweight and obesity.

Following the progress of hypertension is an important concept because the pediatrician can identify children at a higher risk of becoming adults with hypertension. Pediatricians can thus initiate preventive measures at an early age.
Determinants of blood pressure

Blood pressure is determined by the interaction of genetic and environmental factors.

The predominant theory about genetics in hypertension is that hypertension may result from one or more abnormalities in a complex set of systems - electrolyte transport, sympathetic and endocrine control mechanisms - that may each have potential genetic changes. The occurrence of alterations in some of these genes or a combination of alterations may result in clinical manifestation of hypertension. The fact that the expression of hypertension in the population, as a polygenic disease, is not distributed as present or absent, but as continuous, without clear limits between normal and abnormal, contributes to this hypothesis. Studies conducted in the pre-molecular era suggested that hereditary factors contributed to at least 20 to 50% of the variation of blood pressure in humans.

In the adult population, prevalence, morbidity and mortality rates are higher among black people. The same has not been clearly established for childhood hypertension yet. Therefore, although blood pressure tends to be higher in black than in white children, the difference does not seem to be clinically relevant when data are corrected for body size and sexual maturation. Moreover, black adolescents, particularly boys, have a less marked nocturnal decline in blood pressure measured by ABPM.

Environmental factors are as important as genetic factors in predicting blood pressure levels along an individual’s life. The association of genetic and environmental factors starts as early as in the prenatal period.

Epidemiological studies show that there is a greater incidence of hypertension and death due to cardiovascular problems for adults who were born small and grew slowly during the first year of life. Barker et al. were the first to suggest this association. They evaluated men born between 1911 and 1930 in six boroughs of Hertfordshire, England, and noted an association between the increase in deaths due to cardiovascular causes and low birthweight and small head circumference at birth. This concept became known as the Barker hypothesis. The newborn’s weight seems to have a prognostic value for blood pressure levels in all age groups, from childhood to old age.

These findings suggest that one or more perinatal factors, probably associated with maternal and/or fetal nutrition, may permanently affect physiological factors and predispose the individual to a higher risk of cardiovascular disease later in life. The factors that may be involved are a diet poor in protein during pregnancy, the renin-angiotensin system, and use of glucocorticoids.

Dietary factors

Sodium

There is a well-documented association between sodium intake and hypertension in animals and human beings. Dahl et al. demonstrated, in an animal model studied over 30 years ago, that sodium intake, associated with a genetic factor, led to a rapid increase in blood pressure. A large multicenter study conducted by the Intersalt Cooperative Research Group found a positive correlation between sodium intake (estimated by 24-hour urinary excretion of sodium) and blood pressure after adjustment to age, sex, body mass index, potassium and alcohol intake. They studied 10,079 people, 8,344 of whom were normotensive, with ages ranging from 20 to 59 years. The correlation was observed in 48 of the 52 populations studied, and was also positive for individuals in the same community.

Cutler et al. conducted a meta-analysis of 32 random clinical studies with 2635 individuals, and found reductions of 4.8 and 2.5 mmHg in systolic and diastolic pressure, respectively, when sodium was reduced in the diets of hypertensive patients. The reduction was less marked, 1.9 and 1.1 mmHg, in normotensive individuals. Moreover, linear regression revealed a dose-response relationship. Another meta-analysis study reached the same conclusion - salt restriction was effective in individuals with hypertension, but had a small, non-significant effect in normotensive individuals.

Falker & Michel investigated the effect of dietary salt in the blood pressure of children and adolescents. They conducted a review of literature and demonstrated that dietary salt restriction was more effective in patients with a family history of hypertension and in obese patients than in the general population.

Hofman et al. conducted a random double-blind study and found higher blood pressure levels at 6 months in 245 children that were fed regular milk formula than in the 231 that received a low sodium intake formula. These data suggest that the effect of sodium on blood pressure may start still in infancy.

In a recent publication, Singhal et al. evaluated the effect of diet during the neonatal period in the blood pressure of adolescents (13-16 years) who were premature at birth. They found that blood pressure levels were lower who had been breastfed than in those who had been formula fed. No difference was observed regarding whether individuals had been premature or born at term, which suggests that postnatal diet may also contribute to higher blood pressure levels in this population.

However, high sodium intake is not enough for the onset of hypertension, as demonstrated by the fact that not all individuals that consume high amounts of dietary sodium develop hypertension. Such phenomenon, known as sodium sensitivity, is more frequent in patients with severe
hypertension, in black individuals, in patients with a family history of hypertension, in the elderly, and in patients with hyperaldosteronism.31

**Potassium**

Results reported by several authors suggest that low dietary potassium intake may play an important role in the genesis of hypertension. Elliot et al., in the Intersalt Group, noted a negative independent correlation between potassium urinary excretion and interpopulation variation of hypertension.32

Their meta-analysis of randomized clinical trials demonstrated that potassium supplementation is associated with significant reductions in systolic and diastolic pressure.33,34

A study with children and adolescents aged 5 to 17 years followed up for 7 years revealed that the sodium/potassium ratio in diet has a more serious effect on a child’s blood pressure than sodium intake alone.35

**Obesity**

Obesity is one of the most common chronic health problems in contemporary society. In the United States, more than 50% of all adults are classified as obese or overweight. Obesity rates for Americans 12 to 17 years old range from 13% to 36%, and overweight rates range from 4% to 12%, depending on sex and race. In Brazil, the prevalence of obesity has increased significantly in the last decades.37

The association of obesity and hypertension may also be found early in childhood, and has significant clinical importance because of its association with silent diseases, such as dyslipidemia, type II diabetes mellitus, and insulin resistance syndrome.6

**Stress**

Individuals exposed to repeated psychological stress run a higher risk of developing hypertension. Genetic factors also affect the response to stress: children of hypertensive individuals have a higher increase of blood pressure levels in response to stressing factors.

**Other factors**

Other factors, such as a sedentary life style, smoking, and alcohol drinking, may also affect blood pressure.

**Etiology**

The main causes of hypertension by age group are described below.6

**Newborns:**
- renal artery thrombosis;
- renal artery stenosis;
- renal venous thrombosis;
- congenital renal abnormalities;
- coarctation of the aorta;
- bronchopulmonary dysplasia (less frequent);
- patent ductus arteriosus (less frequent);
- intraventricular hemorrhage (less frequent).

**First year of life:**
- coarctation of the aorta;
- renovascular disease;
- renal parenchymal disease.

**From 1 to 6 years:**
- renal parenchymal disease;
- renovascular disease;
- coarctation of the aorta;
- essential hypertension;
- endocrine causes (less frequent).

**From 6 to 12 years:**
- renal parenchymal disease;
- renovascular disease;
- essential hypertension;
- coarctation of the aorta;
- endocrine causes (less frequent);
- iatrogenic causes (less frequent).

**From 12 to 18 years:**
- essential hypertension;
- iatrogenic causes;
- renal parenchymal disease;
- renovascular disease (less frequent);
- endocrine causes (less frequent);
- coarctation of the aorta (less frequent).

In young children (younger than six years) hypertension is more likely to be secondary, while by the end of the first and beginning of the second decade of life, essential hypertension gradually becomes the predominant etiology.

**Investigation**

Etiologic investigation should be conducted when a diagnosis of hypertension is made in a child. The younger the child and the higher the blood pressure levels, the higher the chances of secondary hypertension, which should thus be thoroughly investigated. The Task Force has provided an excellent algorithm for such investigation.
Investigation should begin with a detailed clinical history, focusing on factors that lead to hypertension. Some of the important aspects to be approached are:

- prenatal and delivery history – birthweight, fetal distress, neonatal anoxia, umbilical catheterization, etc.
- symptoms suggestive of hypertension – headache, vomiting, scotoma, etc.
- present or past renal and urological disease, such as urinary infections;
- use of medication – nasal or oral vasoconstrictors, corticoids, contraceptives;
- symptoms suggestive of endocrine causes, such as weight loss, sweating, tachycardia, heart palpitation, fever, cramps, weakness;
- family history of essential hypertension and its complications, or genetic disease associated with secondary hypertension, such as polycystic disease.

Physical examination is also very important. Some of the procedures listed below may aid in the diagnosis of secondary hypertension:

- measurement of blood pressure in the arms and the legs, and careful detection of pulses in arms and legs, which may aid in the diagnosis of coarctation of the aorta;
- findings suggestive of ambiguous genitalia, which may suggest congenital adrenal hyperplasia;
- physical signs suggestive of genetic disease, such as neurofibromas and cafe-au-lait spots in neurofibromatosis;
- signs suggestive of endocrine causes - central obesity, moon facies, striae, hirsutism, enlarged thyroid gland, etc.;
- signs of renal or renovascular disease - kidney mass or enlarged kidneys, edema, abdominal bruit.

The examination of the fundus of the eye, which provides direct visualization of the retina blood vessels and the identification of possible angiopathy due to hypertension, is another important procedure during physical examination, and should be performed by an experienced observer.

The 1996 Update on the Task Force recommended that the investigation of hypertension be made in different phases (Table 1). The first phase should be performed in all children with hypertension. Some of the main causes of secondary hypertension, target organs damage, and risk factors for cardiovascular disease should be investigated. About 60 to 80% of the cases of secondary hypertension are caused by renal parenchymal diseases. Severe elevations of blood pressure levels, no matter at what age, should be more thoroughly investigated. Mild hypertension, in turn, is not usually associated with a secondary disease. Follow-up programs to detect secondary causes of hypertension in adolescents have yielded a low diagnostic index. Therefore, it has been suggested that asymptomatic adolescents with mild hypertension should undergo only basic examinations (phase 1).

It should be pointed out here that echocardiography is more sensitive than electrocardiography in the early detection of left ventricle hypertrophy secondary to hypertension.

The second and third phases of the investigation are more aggressive and should be performed in infants - in the first year of life, all hypertension is potentially secondary – with elevated blood pressure levels, or with target organ damage identified in phase 1, such as left ventricle hypertrophy. Examinations should be performed according to each patient’s clinical history. For example, a patient with a history of peaking hypertension with heart palpitations, tachycardia, and sweating should undergo investigation of catecholamine dosage, while a patient with a history of repeated urinary tract infections should first undergo renal scintigraphy and voiding urothrocystography (renal scar? vesicoureteral reflux?).

Renovascular disease is one of the most frequent and serious causes of secondary hypertension in children. It is a serious disease, but treatment can improve and even cure it. About 5 to 25% of children with secondary hypertension have renovascular disease. Young children with severe elevations of blood pressure are the most likely to have renovascular disease. These patients have high levels of renin either in circulation or in renal veins. Fibromuscular dysplasia is the most common cause of renovascular hypertension in childhood.

The diagnosis of renovascular hypertension is the most difficult part of the investigation because it requires the use

### Table 1 - Investigation of hypertension in childhood and adolescence proposed by the 1996 Update of the American Task Force

<table>
<thead>
<tr>
<th>Phase</th>
<th>Procedure</th>
</tr>
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</table>
| Phase 1 | Complete blood test  
Urinalysis and urine culture  
Urea, creatinine, electrolytes, calcium and uric acid  
Fasting glycemia  
Lipid profile  
Renal ultrasonography  
Echocardiogram |
| Phase 2 | DMSA and miccional urethrocystography  
Renal scintigraphy (with and without captopril)  
Renin level with and without loop diuretic  
Serum aldosterone  
Catecholamine in 24-hour urine  
Serum and urinary steroids |
| Phase 3 | Renal arteriography and renin level in renal vein  
Scintigraphy with meta-iodobenzylguanidine (MIBG)  
Catecholamine in vena cava  
Renal biopsy |

Source: National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents.
of invasive methods, such as renal arteriography with collection of renin in renal vein, to confirm diagnosis. Other less invasive methods have been suggested to identify renal artery disease in adults, such as renal Doppler ultrasound, magnetic resonance angiography, and spiral computed tomography. In children, particularly in infants, whose vessels are small, the usefulness of these examinations has not been proven. Renal scintigraphy, (DMSA, DTPA and MAG3), with and without angiotensin-conversion enzyme inhibitors (ACEIs), seems to be useful, but more recent studies have suggested that its sensitivity and specificity are limited in childhood. Therefore, the question remains for the clinician: When should renal arteriography be performed in children with hypertension? Shahdadpuri et al. suggest that it should be performed in every child with severe hypertension and whose condition has not been effectively controlled with the administration of one single drug. Tyagi et al., in a recent study with 35 children that underwent percutaneous angioplasty, reported cure of hypertension in one third of the patients, and improvement in 50%. Restenosis occurred in 25% of the cases, but mostly in patients with Takayasu arteritis.

**Treatment**

The objectives of treatment are to reduce blood pressure to below the 90 percentile and to prevent late complications of hypertension. Treatment should include pharmacological and non-pharmacological measures.

**Non-pharmacological treatment**

Non-pharmacological treatment aims to reduce morbidity and cardiovascular mortality by means of changes in life style.

It is recommended for all individuals with hypertension, as well as for normotensive individuals with high cardiovascular risk. Of these changes, those that effectively reduce blood pressure are obesity prevention, reduction of salt intake and alcohol drinking, regular physical exercise, and no use of drugs that elevate blood pressure. The reasons why life style changes are useful are:

- low cost and minimum risk;
- blood pressure reduction;
- increased efficacy of medication; and
- reduction of cardiovascular risk.

In patients with high-normal or borderline blood pressure (systolic or diastolic pressure between 90 and 95 percentiles), treatment consists of changes in life style and regular monitoring of blood pressure. Some studies have demonstrated that, besides reducing blood pressure levels, reduction of dietary salt also reduces mortality due to cerebral vascular accident and regression to left ventricular hypertrophy. Salt restriction may also reduce urinary calcium excretion, thus contributing to the prevention of osteoporosis in the elderly. Therefore, dietary salt restriction is recommended not only for individuals with hypertension, but also for the general population.

This recommendation should be for a daily intake of 100 mEq (6 g of salt = 1 teaspoonful). In practical terms, individuals should avoid the ingestion of processed foods, such as canned, preserved, cured and smoked foods. Patients should be advised to use minimum amounts of salt in the preparation of meals, and to avoid having a salt shaker on the table during meals. The use of salt substitutes containing potassium chloride instead of sodium chloride may be recommended to patients, though some may find its taste a limiting factor. An interval of at least 8 weeks is required for the maximum hypotensive effect of salt restriction to be observed.

Weight reduction has been shown to be effective in the treatment of hypertension in obese children and adolescents. General recommendations for weight reduction include dieting and physical activity programs. To maintain the desired weight, an individualized dietary program is required, with particular attention to social, economic and cultural factors and to the patient’s motivation. However, weight reduction at this age, as well as in adults, is very difficult to attain.

Aerobic physical exercises aid in weight loss and in the reduction of systolic and diastolic pressure.

During exercises, blood vessels in muscles and skin dilate, and peripheral vascular resistance is reduced. Systolic pressure may tend to increase because of decreased cardiac output, but vasodilatation may lead to the maintenance or even reduction of blood pressure in some individuals.

Hypertension is the most common cardiovascular disorder in athletes. Hypertension does not increase the risk of sudden death, but there are reports of cerebral vascular accidents that may have been caused by hypertension during exercise. For this reason, in 1997 the American Academy of Pediatrics published a normative guide for sports activities for children and adolescents with hypertension. Its recommendations were:

- significant hypertension (95–99 percentile) without target organ damage: no restriction to sports activities, and BP should be measured every two months;
- severe hypertension (> 99 percentile or > 20% above 95 percentile) without target organ damage: restricted sports activities until BP is controlled;
- young athletes with hypertension: promote healthy habits, such as avoiding the use of androgens, growth hormones and drugs, particularly cocaine, as well as smoking and high sodium intake.

**Pharmacological treatment**

It is still unclear at what age or which is the adequate moment to initiate pharmacological treatment in pediatric patients with hypertension. Data from longitudinal follow-
ups of children and adolescents at risk for the development of cardiovascular disease are not available. It is unclear whether hypertensive therapy initiated in childhood or adolescence results in a significant reduction of risk, when these patients are compared with patients that initiate treatment later in life.\textsuperscript{12}

Pharmacological treatment of hypertension in childhood and adolescence is recommended in the following cases:

- secondary hypertension;
- symptomatic hypertension;
- hypertension with target organ damage;
- severe hypertension: when blood pressure levels are 20% above the 95 percentile;
- hypertension that does not improve with non-pharmacological treatment.

It is equally important to mention that only a few drugs have been tested in children. Anti-hypertensive therapy is initiated at dosages extrapolated from pharmacokinetic data obtained in studies with adults.\textsuperscript{41} In the United States, several drugs have been studied for the pediatric population since FDA norms were updated.\textsuperscript{42}

**Calcium channel blockers:** the use of short-acting nifedipine has been broadly discussed; this is the first drug to be widely used in children, mainly because of its rapid action. Uncontrolled hypotension associated with cardiac events in adults has led to the recommendation to abandon its use. However, Blaszak et al. demonstrated that the fall in blood pressure may be controlled with the reduction of the initial dose and careful monitoring,\textsuperscript{43} but the use of nifedipine, even in hypertensive crisis, is being phased out because of the availability of other drugs.

**ACEIs:** even though it had been used for two decades until the year 2000, no drug in this group has been approved for use in hypertensive children. The first drug in this group to be approved by the FDA was enalapril, which is well tolerated but may cause coughing. Other drugs, such as ramipril, have already shown to be effective and are under analysis for approval. Some angiotensin receptor blockers were approved for use in adults (losartan and irbesartan), but have not been thoroughly studied for use in children.\textsuperscript{12}

The most frequent drug dosages for the treatment of hypertension in children, as well as their main side effects, are shown in Table 2.

### Table 2 - Antihypertensive drugs frequently used in children\textsuperscript{5,6,12}

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypertensive emergency</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>0.25–0.5 mg/kg/dosage O every 6 h</td>
<td>(\uparrow) heart frequency, headache, vertigo</td>
</tr>
<tr>
<td>Sodic nitropusside</td>
<td>0.5–8 (\mu)g/kg/min IV</td>
<td>Vasodilator, beginning of immediate effect</td>
</tr>
<tr>
<td>Labetalol</td>
<td>1–3 mg/kg/h IV</td>
<td>Alpha and beta block</td>
</tr>
<tr>
<td>Esmolol</td>
<td>50–300 (\mu)g/kg/min IV</td>
<td></td>
</tr>
<tr>
<td>Nicardipine</td>
<td>1–3 (\mu)g/min IV</td>
<td>Calcium channel blocker, effect in the hypertensive crisis</td>
</tr>
<tr>
<td><strong>Chronic treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>infants: 0.03–2.0 mg/kg/day O every 12 h, children: 1.5–6.0 mg/kg/day O every 8 h</td>
<td>(\uparrow) K, (\downarrow) platelet, neutropenia, cough, caution in the renal artery stenosis, GFR</td>
</tr>
<tr>
<td>Enalapril</td>
<td>0.15–7 mg/kg/day O every 12-24 h</td>
<td>(\downarrow) GFR, (\uparrow) K, (\downarrow) platelets, (\downarrow) LEU</td>
</tr>
<tr>
<td>Nifedipine retard</td>
<td>0.25–3 mg/kg/day O every 12 h</td>
<td>(\uparrow) heart frequency, headache, vertigo</td>
</tr>
<tr>
<td>Anlodipine</td>
<td>0.1–0.6 mg/kg/dosage 1 to 2 times/day</td>
<td>Calcium channel blocker, well tolerated, efficient in patients with CRF</td>
</tr>
<tr>
<td>Isradipine</td>
<td>0.15–0.5 mg/kg/dosage 3 to 4 times/day</td>
<td>Calcium channel blocker</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>1–3 mg/kg/day O every 12 h</td>
<td>To monitor (\downarrow) K, (\uparrow) Glu, (\uparrow) uric acid</td>
</tr>
<tr>
<td>Furosemide</td>
<td>1–12 mg/kg/day O every 6–12 h</td>
<td>To monitor (\downarrow) K, (\uparrow) Glu, (\uparrow) uric acid, hypercalciuria</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>0.02–0.3 mg/kg/day O every 6–12 h</td>
<td>To monitor (\downarrow) K, (\uparrow) Glu, (\uparrow) uric acid</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>1–3 mg/kg/day O every 12 h</td>
<td>Aldosterone antagonist</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>0.75–3.0 mg/kg/day O every 6–8 h</td>
<td>(\uparrow) heart frequency, headache, lupus like syndrome (rare in pediatrics)</td>
</tr>
<tr>
<td>Minoxidil</td>
<td>0.1–1.0 mg/kg/day O every 12 to 24 h</td>
<td>Retention of salt and water, hirsutism</td>
</tr>
<tr>
<td>Prazosin</td>
<td>0.05–0.5 mg/kg/day O every 8 to 12 h</td>
<td>To give the first dosage while the patient is lying</td>
</tr>
<tr>
<td>Propranolol</td>
<td>1–8 mg/kg/day O every 6–12 h</td>
<td>Forbidden in patients with asthma and CHF, (\uparrow) Glu</td>
</tr>
<tr>
<td>Atenolol</td>
<td>1–8 mg/kg/day every 12–24 h</td>
<td>Bronchospasm and bradycardia</td>
</tr>
</tbody>
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Adapted from: Kay et al.,\textsuperscript{14} Bartosh SM & Aronson A,\textsuperscript{6} and Nehal US & Ingelefinger JR\textsuperscript{12}
Consequences of childhood hypertension

Autopsy data from the Bogalusa Heart Study revealed a significant association between risk factors (elevated body mass index, hypertension, smoking, and high LDL-cholesterol and triglycerides levels) and arteriosclerotic lesions in children and young adults that died in accidents. Arteriosclerosis - pathological changes that are usually believed to be an adult problem - may well begin very early in life, in childhood.44

Another consequence of hypertension in children is left ventricular hypertrophy (LVA). There is a direct association between blood pressure and the size of the left ventricle in normotensive children - cardiac size increases with the increase in blood pressure percentile. Moreover, children and adolescents with essential hypertension have an increased prevalence of abnormal left ventricular geometry. Although this change seems to be an adaptation, concentric left ventricle hypertrophy is a significant and independent risk factor for cardiac mortality. Fortunately, this hypertrophy can regress with the treatment of hypertension, which has been demonstrated in studies with adults.45

In conclusion, the effects of several risk factors, such as hypertension, that may lead to coronary arteriosclerosis begin in childhood. For this reason, the pediatrician should pay special attention to the diagnosis and treatment of hypertension and other cardiovascular risk factors early in childhood. We will thus have healthier children today and a healthier adult population in the future.

References

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