Consensus Document

Practical Recommendations for the Diagnosis, Investigation and Management of Hypertension in Children and Adolescents: Hellenic Society of Hypertension Consensus Document

George S. Stergiou[1], Andriani Vazeou[2], Constantinos J. Stefanidis[3], Anastasios Kapogiannis[4], Dimitrios Georgakopoulos [5], Stella Stabouli[6], Stella Douma[7], Michalis Doumas[7], Pantelis Zebekakis[8], Thomas Makris[9], Costas P. Tsioufis[10], Athanasios Manolis[11]; for the Hellenic Society of Hypertension

[1]Hypertension Center, Third University Department of Medicine, Sotiria Hospital, Athens, [2]First Department of Pediatrics, "P. & A. Kyriakou" Children's Hospital, Athens, [3]Department of Nephrology, "P. & A. Kyriakou" Children's Hospital, Athens, [4]Department of Nephrology, "Agia Sophia" Children's Hospital, Athens, [5]Department of Cardiology, "P. & A. Kyriakou" Children's Hospital, Athens, [6]Pediatric Intensive Care Unit, Hippokration Hospital, Thessaloniki, [7]Second University Department of Medicine, "Hippokration" Hospital, Thessaloniki, [8]First University Department of Medicine, "AHEPA" Hospital, Thessaloniki, [9]Department of Cardiology, "Helena Venizelou" General Maternity-District Hospital, Athens, [10]First University Department of Cardiology, "Hippokration" Hospital, Athens, [11]Department of Cardiology, "Asklipiion" Hospital, Athens, Greece

Key words: **Blood pressure, pediatric, guidelines, treatment.**

Manuscript received: August 4, 2012;
Accepted: November 21, 2012.

Address:
George S. Stergiou
Hypertension Center
Third University Department of Medicine
Sotiria Hospital
152 Mesogion Avenue
115 27 Athens, Greece
e-mail:
gstergi@med.uoa.gr

In the last decade there has been a considerable change in attitudes towards hypertension in children and adolescents.[1,2] First, it is recognized that mild elevation of blood pressure in children and adolescents is more common than previously believed. Second, accumulating evidence suggests that in the past two decades mean blood pressure, and consequently the prevalence of hypertension in children and adolescents, is rising.[3] This rise is mainly attributed to the increasing prevalence of obesity among children and adolescents.[4-6] However, other aspects of the modern lifestyle might contribute, such as reduced physical activity and the increasing time that children spend in front of a screen (television or personal computer).[4] Moreover, longitudinal studies have shown that elevated blood pressure during childhood and adolescence often progresses to hypertension in adult life (tracking), which has both epidemiologic and clinical impact.[7-9] Thus, it seems that primary hypertension in adults often has its roots in childhood and adolescence.[1,2,10] Several studies have documented the familial aggregation of essential hypertension, with close associations reported for both father-offspring and mother-offspring systolic blood pressure.[11] However, when the mother had a history of hypertension there was a larger proportion of offspring in the highest blood pressure quartile, suggesting a key role of the mother in the development of essential hypertension.[11]

The development of knowledge about and attitudes towards hypertension and its management has major differences in relation to children and adolescents compared to adults. In children, since hypertension-induced cardiovascular complications take too many years to occur, it is not feasible to conduct outcome studies that examine the association of blood

pressure with cardiovascular risk, as was done in adults. Therefore, the management of hypertension in children is not founded on the concept of "evidence-based medicine", but on expert consensus guidelines and extrapolation of evidence from studies in adults. Despite the inadequate evidence related to pediatric hypertension, the development of recommendations is necessary in order to guide physicians in the management of high blood pressure in clinical practice. Detailed guidelines for hypertension in children and adolescents have been published in Europe[1] and the US.[2]

Both the American and the European guidelines recommend that blood pressure measurement should be part of the routine evaluation of all children above the age of 3 years.[1,2] Blood pressure should preferably be checked once per year, particularly in children at high risk for development of cardiovascular disease and accelerated atherosclerosis, including children whose parents have hypertension or premature coronary heart disease (father <55 years or mother <65 years), and children who are overweight or obese, or have dyslipidemia (particularly in the presence of obstructive sleep apnea or a sedentary lifestyle), diabetes mellitus, or nephropathy.[12,13]

In the last few years, the implementation of this recommendation in clinical practice has had the following consequences: (i) it is recognized that elevated blood pressure is not uncommon, especially in adolescents; (ii) many cases of hypertension that in the past would have remained undiagnosed for many years are diagnosed early; and (iii) diagnostic problems due to blood pressure variability and the white-coat and masked hypertension phenomena are common.

This article is addressed to pediatricians, internists, cardiologists, and general practitioners who deal with elevated blood pressure in children and adolescents. The objective is to provide essential and practical information and guidance on the diagnosis, evaluation and management of hypertension in children and adolescents, with a focus on primary hypertension, which is the most common cause of hypertension in adolescents. Secondary hypertension and hypertension emergencies are not discussed because these are tasks for specialized physicians.

Causes of hypertension

The causes of hypertension in children and adolescents are similar to those in adults. Nevertheless, secondary hypertension is more common in children than in adolescents, particularly in young children and those with stage 2 hypertension.[1,2,14] The younger the age, the higher the chance of identifying an underlying cause of hypertension that might be treatable. In children under the age of 12 years, renal disease and renovascular hypertension are the most common causes,[1,2,14] followed by aortic coarctation and primary hypertension. Endocrine causes, such as pheochromocytoma, primary aldosteronism, Cushing syndrome, etc., are rare. On the other hand, after the age of 12 years primary hypertension is the most common cause and is characterized by elevation of systolic blood pressure only, or both systolic and diastolic blood pressure.[1,2,14] In the last years the association of hypertension with obstructive sleep apnoea has been recognized, which is not uncommon, particularly in obese children and adolescents.[15]

Blood pressure measurement and diagnosis of hypertension

For the reliable evaluation of children with elevated blood pressure and the accurate diagnosis of hypertension it is necessary to have repeated office blood pressure measurements and 24-hour ambulatory blood pressure monitoring.[1,2,16-18] Unfortunately, in clinical practice blood pressure is not always carefully evaluated and this might result in an incorrect diagnosis of hypertension (overdiagnosis) and unnecessary investigation, thereby causing considerable discomfort to the child and family, and a waste of healthcare resources. Underdiagnosis of hypertension due to incorrect evaluation of blood pressure may also occur in children. The most common problems in the evaluation of blood pressure in children and adolescents are presented in Table 1. It is important to mention that in children and adolescents the use of normalcy tables providing percentile blood pressure values according to age, gender, and height is necessary for the interpretation of office and out-of-office blood pressure measurements (Tables 2-5).[1,2,16-19]

Office blood pressure measurement

In children with possible hypertension, blood pressure should be carefully measured in the office by the doctor or nurse on at least 2-3 visits, with 2-3 measurements per visit.[1,2,16] The first and often the second office visit might give higher and unstable blood pressure values. Although the conventional office measurement remains the cornerstone for the as-

Table 1. Common problems in the evaluation of blood pressure in children and adolescents.

- Inappropriate measurement conditions (stress, exercise, without a few minutes' rest, etc.).
- Inappropriate cuff size according to the child's arm circumference.
- Diagnosis of hypertension based on blood pressure measurement from a single office visit.
- Diagnosis based on blood pressure measurements obtained by an automated electronic (oscillometric) device (not confirmed by auscultation).
- Inappropriate use of blood pressure thresholds for hypertension diagnosis according to age, gender and height.
- No confirmation of hypertension diagnosis by ambulatory blood pressure monitoring.
- Ambulatory blood pressure monitoring not performed on routine school day (i.e. performed during hospitalization or while the child remains at home).

sessment of blood pressure, in children and adolescents 24-hour ambulatory blood pressure monitoring is mandatory to confirm the diagnosis of hypertension.[1,16,18]

For office blood pressure measurement in children, a standard mercury sphygmomanometer or a validated aneroid manometer and the auscultatory method should be used.[1,2] It is noted that for environmental reasons mercury sphygmomanometers are being banned from clinical use and will soon not be available. The automated electronic (oscillometric) devices have the advantage of eliminating observer bias and error, yet they may not be accurate and require separate validation in children. Unfortunately, few of them have been adequately tested in children and proved to be accurate. Lists of validated oscillometric devices are available on the internet (see www.dableducational.org, www.bhsoc.org). Elevated blood pressure in children detected using an electronic device should be confirmed by taking measurements with a device that uses the auscultatory method.[1,2]

The selection of a cuff of appropriate size according to the individual child's arm circumference is essential for accurate blood pressure measurement. The length of the bladder (the inflatable part of the cuff) should encircle 80-100% of the arm circumference and its width should be about 40% of that (4 × 8 cm, 6 × 12 cm, 9 × 18 cm, 10 × 24 cm).[1,2,20,21] A large cuff applied on a small arm (i.e. adult cuff applied in children) may result in underestimation of blood pressure by up to 30 mmHg.[20,21] On the other hand, a small bladder applied to a big arm (i.e. a small cuff applied to an obese adolescent arm) might overestimate blood pressure by up to 30 mmHg.[20,21] The Korotkov sound I (when the first rhythmic sound appears) is used to estimate systolic blood pressure and sound V (when the sounds disappear) is used for diastolic blood pressure. When the sounds persist up to 0 mmHg the Korotkov sound IV (when the sounds become muffled) is used to estimate diastolic blood pressure.

Diagnostic criteria of hypertension

The criteria for the diagnosis of hypertension in children are based on the concept that blood pressure increases with age and body size. It is, therefore, inappropriate to use the same threshold to define hypertension in all children. Thus, although in adults the blood pressure threshold for hypertension is the same, regardless of the age, gender and somatometric characteristics (systolic >140 mmHg and/or diastolic >90 mmHg), in children and adolescents the diagnostic threshold differs according to the individual's age, gender and height. For the evaluation of office measurements, blood pressure percentiles derived from studies in the US that included data from 63,000 children and adolescents aged 1-17 years are used (Tables 2a and 2b).[1] According to the latest US[2] and European[1] guidelines, an office blood pressure below the 90th percentile (according to age, gender and height) is considered as normal, and one between the 90th and 95th percentile as high-normal[1] (or prehypertension in the US guidelines)[2] (Table 3). In adolescents, blood pressure is considered as high-normal if it is higher than 120/80 mmHg, even if this is below the 90th percentile.[1,2] Office blood pressure between the 95th and 99th percentile plus 5 mmHg is considered as stage 1 hypertension and higher than that as stage 2 (Table 3).[1,2]

Twenty-four-hour ambulatory blood pressure monitoring

Twenty-four-hour ambulatory blood pressure monitoring is considered indispensable for the diagnosis of hypertension in children.[1,2,18] Ambulatory blood pressure monitoring is also useful after treatment initiation for the evaluation of resistant hypertension, for the assessment of 24-hour blood pressure control in children with target organ damage, and when overtreatment is suspected.[1,2,18] Moreover, ambulatory blood pressure is mandatory for the detection of

Table 2a. Percentiles for office blood pressure in boys according to body height (reproduced from reference #2, with permission).

Age (year)	Blood pressure percentile	Systolic blood pressure (mmHg) Percentile of height							Diastolic blood pressure (mmHg) Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
1	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
2	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
3	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
4	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
5	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
6	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
7	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
8	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
9	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
10	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
11	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
12	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
13	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
14	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
15	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
16	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
17	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

Table 2b. Percentiles for office blood pressure in girls according to body height (reproduced from reference #2, with permission).

Age (year)	Blood pressure percentile	Systolic blood pressure (mmHg) Percentile of height							Diastolic blood pressure (mmHg) Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
1	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
2	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
3	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
4	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
5	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
6	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
7	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
8	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
9	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
10	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
11	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
12	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
13	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
14	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
15	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
16	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
17	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

Table 3. Classification of blood pressure in children and adolescents (reproduced from reference #1, with permission).

	Percentile for systolic and/or diastolic blood pressure
Normal	<90th percentile
High-normal	>90th and <95th percentile. In adolescents ≥120/80 mmHg even if <90th percentile
Hypertension stage 1	95th to 99th percentile plus 5 mmHg
Hypertension stage 2	>99th percentile plus 5 mmHg

"white-coat hypertension" (elevated office and low ambulatory blood pressure), "masked hypertension" (low office and elevated ambulatory blood pressure), and the "non-dipping" pattern (nighttime blood pressure declines by less than 10% compared to daytime levels).[1,18,22-25] An ambulatory blood pressure monitor that has been validated in children should be selected, together with a cuff of appropriate size according to the individual's arm circumference. Few ambulatory monitors have been successfully validated in children (lists of validated devices may be found at www.dableducational.org and www.bhsoc.org). Ambulatory monitoring should be performed on a routine, preferably school day. The results are evaluated by calculating the daytime and nighttime blood pressure average. As in the case of office blood pressure measurements, ambulatory blood pressure in children is evaluated by using percentile normalcy tables according to gender and height or age, which were derived by a German study from 949 children aged 5-20 years (Table 4).[17,26] Daytime and/or nighttime ambulatory blood pressure values between the 90th and 95th percentile are considered as borderline, while values above the 95th percentile suggest hypertension.[1,2,17,18,26]

Home blood pressure monitoring

Data on the usefulness of home blood pressure monitoring in children are limited.[1,16,27] However, there is evidence that this method is being used in the evaluation of children with hypertension.[28] Preliminary studies have shown that in children home monitoring is useful in the detection of white-coat and masked hypertension.[16,29,30] Automated oscillometric devices are preferred for home blood pressure monitoring. Devices that have been successfully validated in children should be used with a cuff size appropriate for the individual's arm size. Few automated devices for home monitoring have been successfully validated in children (lists of validated devices may be found at www.dableducational.org and www.bhsoc.org). Wrist devices have not been validated in children and should not be used.

Home blood pressure should be monitored on 6-7 routine school days, with duplicate morning and evening measurements after 5 min sitting rest and with one min between measurements.[1,27] Single readings have little diagnostic value and the average of all

Table 4. Percentiles for ambulatory blood pressure (systolic/diastolic) according to body height (reproduced from references #1, #17, & #26, with permission).

	Boys				Girls			
	Daytime		Nighttime		Daytime		Nighttime	
Height (cm)	90th	95th	90th	95th	90th	95th	90th	95th
120	122/80	125/82	103/61	106/63	118/80	120/82	103/63	106/65
125	122/80	125/82	105/61	108/63	119/80	121/82	104/63	107/66
130	122/80	126/82	106/62	110/64	120/80	122/82	106/63	108/66
135	123/80	126/82	108/63	111/65	120/80	123/82	107/63	109/66
140	123/80	126/82	109/63	113/65	121/80	124/82	108/63	110/66
145	124/79	127/81	111/64	114/66	123/80	125/82	109/63	112/66
150	125/79	128/81	112/64	116/66	124/80	126/80	110/63	113/66
155	127/79	130/81	113/64	117/66	125/80	128/82	111/63	114/66
160	129/79	133/81	114/64	118/66	126/80	129/82	111/63	114/66
165	132/80	135/82	116/64	119/66	127/80	130/82	112/63	114/66
170	134/80	138/82	117/64	121/66	128/80	131/82	112/67	115/71
175	136/81	140/83	119/64	122/66	129/81	131/82	113/63	115/66
180	138/81	142/83	120/64	124/66	-	-	-	-
185	140/81	144/84	122/66	125/66	-	-	-	-

measurements should be evaluated. As with office and ambulatory measurements, percentile normalcy tables, which have been derived from a Greek school study of 778 children aged 6-18 years,[19] are used to evaluate home measurements, according to gender and height (Table 5). Home blood pressure values above the 95th percentile suggest hypertension.[1,19] It should be noted that, in contrast to adults, whose home blood pressure and daytime ambulatory blood pressure have similar levels, children and adolescents have a higher daytime ambulatory blood pressure than home blood pressure, probably due to the high level of physical activity of the young individuals during the day.[1,27,29]

White-coat and masked hypertension

"White-coat" or "isolated office" hypertension is defined as blood pressure that is elevated when measured in the office or clinic, while out-of-office blood pressure assessed by ambulatory or home monitoring is normal.[1,2,20,22-24] On the other hand, "masked hypertension" is the reverse phenomenon, and is defined as blood pressure normal in the office and elevated out of the office.[1,18,24,25,30] As is the case in adults, in children and adolescents the white-coat and the masked hypertension phenomena are both not uncommon. Although preliminary evidence suggests that home blood pressure monitoring is useful for the detection of these phenomena in children and adolescents, at present 24-hour ambulatory blood pressure monitoring is considered as an indispensable method for these diagnoses.[1,16,18,27,29,30]

The diagnosis of white-coat or masked hypertension should be confirmed within several weeks or months by repeat office and ambulatory blood pressure measurements. Both phenomena might be associated with preclinical target organ damage (left ventricular hypertrophy), and therefore require careful evaluation by specialized doctors in order to decide whether drug treatment or follow up with non-pharmacological measures is indicated.[1,18,22-25,27]

Table 5. Percentiles for home blood pressure (systolic/diastolic) according to body height (reproduced from references #1 & #19, with permission).

	Boys		Girls	
Height (cm)	50th	95th	50th	95th
120-129	105/64	119/76	101/64	119/74
130-139	108/64	121/77	103/64	120/76
140-149	110/65	125/77	105/65	122/77
150-159	112/65	126/78	108/66	123/77
160-169	115/65	128/78	110/66	124/78
170-179	117/66	132/78	112/66	125/79
180-189	121/67	134/79	114/67	128/80

Clinical and laboratory evaluation

Children found to have blood pressure levels above the 90th percentile should be evaluated with repeated office and out-of-office measurements. If on repeated measurements blood pressure is below the 90th percentile, no further evaluation is required. Children with blood pressure between the 90th and 95th percentile should be followed regularly and lifestyle modification measures should be applied.[1,2] If blood pressure exceeds the 95th percentile, evaluation is required as discussed below.

Medical history and physical examination

In all children with elevated blood pressure, it is essential that detailed information be obtained on family history related to hypertension (parents with hypertension, cardiovascular disease, diabetes mellitus, dyslipidemia, obesity, inherited renal or endocrine disease).[1,2,12] Information should also be obtained on the child's perinatal history (birthweight, months of gestation, problems during pregnancy), history of renal, cardiac, neurologic and endocrine disease, symptoms of secondary hypertension or target organ damage, lifestyle (nutrition, physical activity), and the use of drugs or other substances.[1,2,12,14] Body height and weight should be recorded to calculate the body mass index percentile, and a complete physical examination should be performed with focus on the cardiovascular system (blood pressure measurement on both arms and a leg, cardiac murmurs), neural system, abdomen, and fundoscopy.

Laboratory investigation

Recommended tests for all children with suspected hypertension include: full blood count, serum potassium, sodium, calcium, urea, creatinine, glucose, lipids (total cholesterol, high- and low-density cholesterol, triglycerides), urinary albumin to creatinine ratio, and microscopy, chest-X ray, electrocardiogram, echocardiography and kidney ultrasound.[1,2,14]

The possibility of secondary hypertension should be considered in all children and adolescents with confirmed hypertension. However, the extent of the

evaluation should be individualized for each child. In children with blood pressure slightly above the 95th percentile, extensive evaluation for secondary hypertension is usually not necessary, particularly in adolescents with increased body weight and a family history of hypertension.[1,2] On the other hand, children with sustained blood pressure elevation above the 95th percentile and adolescents with blood pressure above the 99th percentile, or with signs of target organ damage or secondary hypertension, irrespective of age, should be investigated for causes of secondary hypertension. This investigation includes complex and costly tests (hormonal, invasive radiological, nuclear scans, molecular genetics, etc.) and should be performed in specialized centres.

Target organ damage

Hypertension in children and adolescents is not innocent. However, its cardiovascular complications appear after years or decades, and in the vast majority of cases they do not occur during childhood and adolescence. On the other hand, subclinical target organ damage is not uncommon in children with hypertension and can be identified using special techniques.

Echocardiography remains the best established technique for the assessment of hypertension-induced target organ damage in children.[1,2,31,32] Left ventricular mass is calculated on the basis of echocardiographic measurements of the left ventricle, using the Devereux formula.[33] To standardize according to body size, the left ventricular mass is divided by height ($m^{2.7}$) to give the left ventricular mass index.[34] The normal range of this index is uncertain and is based on distribution criteria from relatively small cross-sectional studies (threshold 95-99th percentile).[1,2] Left ventricular hypertrophy appears to be present in about 20-40% of children and adolescents with borderline or sustained primary hypertension.[1,31,35,36] The presence of left ventricular hypertrophy is an indication for antihypertensive drug treatment initiation.[1-2] Therefore, all children with elevated blood pressure should be evaluated with echocardiography.[1-2]

Ultrasonic measurement of carotid intima–media thickness in children has been shown to be associated with dyslipidemia and obesity, as well as with elevated blood pressure, yet currently it is not recommended for routine use in children with hypertension.[1] Estimated glomerular filtration rate using the Schwartz formula and measurement of the urinary albumin-to-creatinine ratio are reliable markers of renal damage in children. In contrast, the role of microalbuminuria in the evaluation of children with primary hypertension remains uncertain, although it often coexists with left ventricular hypertrophy.[1] Fundoscopy is useful for detecting early arterial damage, and it is of great value in accelerated and malignant hypertension with or without encephalopathy.

Management of hypertension

Treatment goals

In adults, the goal of antihypertensive treatment has been established by large interventional outcome studies with hard endpoints of morbidity and mortality. In contrast, in children and adolescents the goal of antihypertensive treatment has been derived from statistical criteria of distribution, as is the case for the blood pressure thresholds for hypertension diagnosis. According to both the American and the European guidelines for pediatric hypertension, the goal of treatment is to reduce blood pressure to below the 95th percentile according to the individual's gender, age and height.[1,2] The European guidelines suggest that "it is probably wiser and safer to aim at a blood pressure <90th percentile", given that a blood pressure in the 90-95th percentile is not considered as normal.[1] In children with chronic renal disease,[2] diabetes mellitus,[1,2] or hypertension-induced target-organ damage,[1] the goal should be <90th percentile. According to the European guidelines, children with chronic renal disease should have a blood pressure goal <75th percentile and in the presence of proteinuria <50th percentile.[1] This recommendation is based on the results of a recent study of 385 children with chronic renal disease who were followed for 5 years, which showed a significant nephroprotective effect of aggressive antihypertensive treatment based on an angiotensin-converting enzyme inhibitor, with concurrent regression of left ventricular hypertrophy.[37]

Non-pharmacological measures – lifestyle modification

The evidence for the efficacy of non-pharmacological measures in reducing blood pressure in children is limited and relevant trials are ongoing. Nevertheless, based on extrapolation of data from adults, it is recommended to apply such measures in children with a high-normal blood pressure (90-95th percentile) who are usually not treated with drugs, as well as in

all children in whom long-term antihypertensive drug treatment is administered.[1,2,12] In children with stage 1 hypertension without preclinical organ damage, nephropathy or diabetes it is recommended to start with non-pharmacological measures for several months (up to one year) before initiating drug treatment.[1,2,12]

Increased body weight is the most important predictor of elevated blood pressure in children and appears to be responsible for more than half of the cases of hypertension in childhood.[3,4] Overweight and obesity in children and adolescents is a major and growing public health issue in several countries, and is accompanied by an increased prevalence of hypertension.[4-6] In children and adolescents with a body mass index above the 95th percentile, a gradual loss of weight (1-2 kg per month) is recommended until body mass index falls below the 85th percentile. Children and adolescents with malignant obesity and target organ damage should be managed by a group of specialists.

Physical exercise has a modest lowering effect on blood pressure in children, and might also help in the management of other cardiovascular risk factors, such as obesity, diabetes and dyslipidemia. Moderate to intense physical exercise is recommended for at least 40 minutes, 3-5 times per week, and has been shown to reduce blood pressure in obese children.[1] In children with stage 2 hypertension strenuous exercise should be discouraged until the blood pressure is reduced. In overweight children it is reasonable to avoid sedentary activities for longer than 2 hours per day. Participation in competitive sports should be restricted only in the presence of uncontrolled stage 2 hypertension.[1]

There are limited data on the effect of dietary changes upon blood pressure in children. However, based on adult studies it is suggested to reduce the consumption of sugar, refreshments, saturated fat and salt. Dietary salt restriction is advised, with daily sodium intake reduced to 1.2 g (corresponds to a daily salt intake of 3.1 g or 53 mEq/day) in 4-8 year old children and 1.5 g in older children (salt intake of 3.8 g/day or 65 mEq/day).[2] A practical way is to start with a no-added-salt diet. This also includes a reduction or elimination of foods containing large amounts of salt (e.g. potato chips, pickles, pretzels, cheese, processed foods). Parents and care providers are encouraged to read food package labels to determine the sodium content of prepared foods and avoid those with a high salt content. An increase in the consumption of fruits, vegetables, fiber, and low-fat dairy products should be encouraged. Concomitant dyslipidemia should be effectively managed, and alcohol as well as smoking should be avoided (including passive smoking).[38]

Antihypertensive drug treatment[1,2,39-51]

The initiation of long-term drug treatment for hypertension in children is a hard decision. Careful confirmation of diagnosis is essential, as well as an evaluation of all relevant parameters and exhaustion of the potential of non-pharmacological measures. It should be mentioned, however, that hypertension in children causes asymptomatic target organ damage, and treatment initiation should not be delayed until such damage occurs.

As mentioned above, children and adolescents with high-normal blood pressure (90th-95th percentile) should not receive antihypertensive drug treatment, but should be regularly followed, with the application of non-pharmacological measures. Blood pressure should be monitored every 3-6 months, and after one year of follow up ambulatory blood pressure monitoring should be repeated before further decision making.[1,2,16,18,40]

Children with hypertension (blood pressure above the 95th percentile) and target organ damage, diabetes, nephropathy, secondary hypertension, or life-threatening hypertension should start treatment immediately after the confirmation of diagnosis.[1,2] Moreover, in all cases with persistent hypertension despite lifestyle modification for several months (up to a year), drug treatment initiation is recommended.[1,2] Lifestyle modification should be continued after the initiation of drug treatment. There is evidence that nonpharmacological and pharmacological therapy in children and adolescents can lead to regression of left ventricular hypertrophy, which is associated with a decrease in abdominal obesity.[37]

Antihypertensive treatment in children should always start with one drug at a low dosage.[1,2] If after several weeks (usually 4-8) blood pressure is not sufficiently decreased, up-titration is recommended. When the blood pressure response is minimal or adverse reactions are observed, it is recommended that the first drug should be replaced with another of a different class.

In general, antihypertensive drugs have not been adequately investigated in children. Thus, their use is mainly based on extrapolation of data from adults. In recent years, efforts have been made by regulatory authorities in the US and Europe, aiming at a more

thorough investigation of antihypertensive drugs in children. As in adults, the first line antihypertensive drugs in children are angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, beta-blockers, calcium-channel blockers and thiazide diuretics.[1,2,39-51] A few comparative trials of these drugs have been conducted in children and showed that they have similar antihypertensive efficacy.[39,41] A review of 27 pediatric studies reported similar antihypertensive effects of angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers and calcium-channel blockers.[41] However, in children with proteinuria, angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers were superior to calcium-channel blockers in reducing the proteinuria.[34,41] Regression of left ventricular hypertrophy has been reported in children treated with an angiotensin-converting enzyme inhibitor or an angiotensin-receptor blocker, combined with a calcium-channel blocker when required.[37] The recommended doses of selected antihypertensive drugs for treatment initiation in children and adolescents are presented in Table 6.[1,2,39-51]

From each drug class the best studied agents are preferred. As in adults, the choice of drug is individualized according to the presence of specific conditions, such as nephropathy, diabetes, etc. In general, the antihypertensive drugs in children are effective at lower doses than those used in adults.

Beta-blockers[1,2,39,40,42-46]

Propranolol, atenolol and metoprolol are the best studied beta-blockers in children, mainly for indications other than hypertension. They are generally well tolerated, with a discontinuation rate of 5%. They are first choice drugs in aortic coarctation and in heart failure. Asthma is a contraindication for their use. Relatively common adverse effects are fatigue and bradycardia.

Angiotensin-converting enzyme inhibitors[1,2,33,39,41,46-49]

Captopril is the most studied drug of this class in children. There are also trials with enalapril, lisinopril, fosinopril, and recently with ramipril, in children with nephropathy. They have a potent antiproteinuric and nephroprotective effect, and are considered first choice drugs in chronic nephropathy, diabetes mellitus and heart failure. They are contraindicated in bilateral renal artery stenosis, in unilateral renal artery stenosis in subjects with a single kidney, in severe hyperkalemia, and in pregnancy (in girls with childbearing potential they should be prescribed only when an effective contraceptive method is being used). The most common adverse effect is dry cough and the most severe but rare adverse effect is angioedema. When administered in children treated with diuretics, the latter should be discontinued for 2-3 days to prevent a hypotensive episode.

Angiotensin-receptor blockers[1,2,39,41,49,50]

Studies in children with hypertension been have recently conducted with losartan, valsartan, irbesartan and olmesartan. These drugs exhibit a strong antiproteinuric effect, stronger than calcium-channel blockers, and independent from their blood pressure-lowering effect. Like angiotensin-converting enzyme inhibitors, they are considered as first choice drugs in chronic nephropathy, diabetes mellitus and heart failure, and are contraindicated in bilateral renal artery stenosis, in unilateral renal artery stenosis in subjects with a single kidney, in severe hyperkalemia, and in pregnancy (in girls with childbearing potential they should be prescribed only when an effective contraceptive method is being used). They have an excellent adverse effect profile, comparable to that of placebo. When administered in children treated with diuretics, the latter should be discontinued for 2-3 days to prevent a hypotensive episode.

Calcium-channel blockers[1,2,39-41,46,51]

Amlodipine is the most well studied agent and few data are available for nifedipine, felodipine, isradipine or verapamil. They are preferred drugs in renal transplant recipients and are contraindicated in heart failure. The most common adverse effect is ankle edema, which is due to vasodilation, does not respond to diuretics and is reduced with the co-administration of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers. They can also cause gingival hypertrophy. Diltiazem and verapamil may cause bradycardia and constipation (mostly verapamil) and have a negative inotropic effect.

Other drugs[1,2,39,40,42-46]

Thiazide diuretics, centrally acting antiadrenergic agents, a1-blockers and direct vasodilators have been used in children for a long time, yet very few studies

Table 6. Recommended doses of antihypertensive drugs in children and adolescents.[1,2,39-51]

Drug class	Drug	Children and adolescents (6-18 years)*			Adults*	
		Dose (mg/kg/day)	Max dose (mg/day)	Doses/day	Dose (mg/day)	Doses/day
Diuretics	Hydrochlorothiazide	0.5-1	50 (3 mg/kg/d)	1	12.5-50	1
	Chlorthalidone	0.3	25 (2 mg/kg/d)	1	12.5-25	1
	Furosemide	0.5-2 mg/kg/dose	6 mg/kg/dose	1-2	20-80	2
	Amiloride	0.4-0.625	10	1	1.25-10	1
	Spironolactone	1.0-3.3	50	1	12.5-50	1
Calcium-channel blockers	Amlodipine	Initial 0.06; up to 0.3 Maintenance 2.5-5†	2.5-5 10	1 1	2.5-10	1
	Felodipine	2.5†	10	1	2.5-20	1
	Isradipine	IR initial 0.05-0.15 mg/kg/dose; up to 0.2 mg/kg/day IR usual 0.3-0.4 mg/kg/d ER 5-10†	- 10 (0.8 mg/kg/d) 10	IR 3 IR 3 ER 1-2	2.5-10	2
	Nifedipine	0.25-0.5	60 (3 mg/kg/d)	1, ER 2, CR 1	30-60	1, ER 2, CR 3
Angiotensin-converting enzyme inhibitors	Captopril	0.3-0.5 mg/kg/dose Adolescents: 12.5-25 mg/dose	6 mg/kg/d 100	2-3 2-3	25-100	2
	Benazepril	Initial 0.2 Maintenance 0.2-06	10 40	1 1	10-40	1-2
	Enalapril	Initial 0.08 Maintenance 0.2-0.6 or 2.5-5†	5 40	1 1	5-40	1-2
	Fosinopril	>50 kg: 5-10† (<50 kg not established)	40	1	10-40	1
	Lisinopril	6-12 years: initial 0.07 (increase up to 0.6) Maintenance 0.2-0.6 or 5-10†	5 40	1	10-40	1
	Quinapril	Initial 5-10†	40	1	10-40	1
	Ramipril	2.5-6†	10	1	5-10	1
Angiotensin-receptor blockers	Candesartan	0.16-0.5 Maintenance 2-16†	32	1-2 1	8-32	1
	Irbesartan	6-12 years: initial 75† >12 years: initial 150†	150 300	1 1	150-300	1
	Losartan	Initial 0.7 Maintenance 25-100†	25-50 100 (1.4 mg/kg/d)	1 1	25-100	1
	Olmesartan	20-35 kg: 10† >35 kg: 20†	20 40	1 1	20-40	1
	Valsartan	Initial 1.3 Maintenance 2	40 160	1 1	80-320	1
Beta-blockers	Atenolol	0.5-1; Maintenance 0.5-1.5	100 (2 mg/kg/d)	1-2	25-100	1
	Bisoprolol	2.5†	10	1	2.5-10	1
	Metoprolol	IR: initial 1-2 ER: initial 0.5-1 Maintenance adjustment based on response	- 50 100 (6 mg/kg/day)	IR 2 ER 1	50-100	1-2
	Propranolol	Initial 1-2; Maintenance 1-5	160 (4 mg/kg/day)	2-3	40-180	2, ER 1
Peripheral Alpha-1 blockers	Doxazosin	1† (unlabeled use)	4	1	1-16	1
	Prazosin	Initial: 0.05-01	15 (0.5 mg/kg/day)	3	2-20	2-3
	Terazosin	Initial: 1†	20	1	1-20	1-2
Central alpha agonists	Clonidine‡	6-12 years: initial 5-10 mcg/kg/d Maintenance 5-25 mcg/kg/d >12 years: initial 0.2† Maintenance 0.2-0.6†	- 0.8 - 0.8	2-3 2-3 2 2	0.1-0.8	2

*The total daily dose should not exceed the maximum recommended dose for adults, which is also provided to facilitate adolescent dosage manipulation. †dose in mg/day. ‡Sudden cessation can lead to severe rebound hypertension. IR – immediate release; ER – extended release; CR – controlled release.

have been conducted with these drugs, mainly involving the empirical use of thiazides. Potassium-sparing diuretics are recommended in primary aldosteronism and contraindicated in renal failure. Loop diuretics are useful in renal and heart failure.

Drug combinations[1,2,39,43,44,46]

A combination of antihypertensive agents is often required in order to achieve optimal blood pressure control in children, particularly in the presence of nephropathy. The combination of two drugs at low doses is often more effective and has fewer adverse effects than a single drug at full dose. In general, free rather than fixed dose combinations are preferred to allow individualized treatment selection. However, fixed combinations are preferred in adolescents in order to improve long-term compliance with treatment. There are no studies of drug combinations in children. Therefore, decision making regarding combination therapy is based on the available evidence in adults. The preferred combinations should probably be those of an angiotensin-converting enzyme inhibitor or an angiotensin-receptor blocker with a calcium-channel blocker or a thiazide diuretic.

Long-term monitoring[1,2]

In the vast majority of cases treatment is lifelong and regular follow up is needed, usually 1-2 times per year. The simplification of the treatment regimen (once-daily 24-hour-acting drugs and fixed-dose combinations when monotherapy fails to control blood pressure) and home blood pressure self-monitoring may improve long-term compliance with treatment, particularly in adolescents. Regular monitoring is also required for other modifiable cardiovascular risk factors (body weight, dyslipidemia, diabetes mellitus, smoking), as well as dietary habits and physical activity (see non-pharmacological treatment).

References

1. Lurbe E, Cifkova R, Cruickshank JK, et al. Management of high blood pressure in children and adolescents: recommendations of the European Society of Hypertension. J Hypertens. 2009; 27: 1719-1742.
2. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004; 114: 555-576.
3. Muntner P, He J, Cutler JA, Wildman RP, Whelton PK. Trends in blood pressure among children and adolescents. JAMA. 2004; 291: 2107-2113.
4. Torrance B, McGuire KA, Lewanczuk R, McGavock J. Overweight, physical activity and high blood pressure in children: a review of the literature. Vasc Health Risk Manag. 2007; 3: 139-149.
5. Kosti RI, Panagiotakos DB. The epidemic of obesity in children and adolescents in the world. Cent Eur J Public Health. 2006; 14: 151-159.
6. Tzotzas T, Krassas GE. Prevalence and trends of obesity in children and adults of South Europe. Pediatr Endocrinol Rev. 2004; 1 Suppl 3: 448-454.
7. Bao W, Threefoot SA, Srinivasan SR, Berenson GS. Essential hypertension predicted by tracking of elevated blood pressure from childhood to adulthood: the Bogalusa Heart Study. Am J Hypertens. 1995; 8: 657-665.
8. Vos LE, Oren A, Bots ML, Gorissen WH, Grobbee DE, Uiterwaal CS. Does a routinely measured blood pressure in young adolescence accurately predict hypertension and total cardiovascular risk in young adulthood? J Hypertens. 2003; 21: 2027-2034.
9. Kollias A, Pantsiotou K, Karpettas N, Roussias L, Stergiou GS. Tracking of blood pressure from childhood to adolescence in a Greek cohort. Eur J Public Health. 2012; 22: 389-393.
10. Lurbe E. Childhood blood pressure: a window to adult hypertension. J Hypertens. 2003; 21: 2001-2003.
11. Fuentes RM, Notkola IL, Shemeikka S, Tuomilehto J, Nissinen A. Familial aggregation of blood pressure: a population-based family study in eastern Finland. J Hum Hypertens. 2000; 14: 441-445.
12. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics. 2011; 128 Suppl 5: S213-256.
13. de Ferranti S, Newburger JW. Risk factors and development of atherosclerosis in childhood. UpToDate, Inc. Wolters Kluwer, Waltham, MA, US. Available at http://www.uptodate.com/contents/risk-factors-and-development-of-atherosclerosis-in-childhood. Accessed 28 July 2012.
14. Lurbe E, Redon J. Secondary hypertension in children and adolescents. In: Mansoor GA, editor. Secondary hypertension. Totowa: Humana Press, 2004. pp. 279-306.
15. Ng DK, Chan C, Chow AS, Chow P, Kwok K. Childhood sleep-disordered breathing and its implications for cardiac and vascular diseases. J Paediatr Child Health. 2005; 41: 640-646.
16. Karpettas N, Kollias A, Vazeou A, Stergiou GS. Office, ambulatory and home blood pressure measurement in children and adolescents. Exp Rev Cardiovasc Ther. 2010; 8: 1567-1578.
17. Soergel M, Kirschstein M, Busch C, et al. Oscillometric twenty-four-hour ambulatory blood pressure values in healthy children and adolescents: a multicenter trial including 1141 subjects. J Pediatr. 1997; 130: 178-184.
18. Urbina E, Alpert B, Flynn J, et al. Ambulatory blood pressure monitoring in children and adolescents: recommendations for standard assessment: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the council on cardiovascular disease in the young and the council for high blood pressure research. Hypertension. 2008; 52: 433-451.
19. Stergiou GS, Yiannes NG, Rarra VC, Panagiotakos DB. Home blood pressure normalcy in children and adolescents: the Arsakeion School study. J Hypertens. 2007; 25: 1375-

1379.
20. O'Brien E, Asmar R, Beilin L, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens. 2003; 21: 821-848.
21. Iyriboz Y, Hearon CM, Edwards K. Agreement between large and small cuffs in sphygmomanometry: a quantitative assessment. J Clin Monit. 1994; 10: 127-133.
22. Sorof JM, Portman RJ. White coat hypertension in children with elevated casual blood pressure. J Pediatr. 2000; 137: 493-497.
23. Sorof JM, Poffenbarger T, Franco K, Portman R. Evaluation of white coat hypertension in children: importance of the definitions of normal ambulatory blood pressure and the severity of casual hypertension. Am J Hypertens. 2001; 14: 855-860.
24. Stabouli S, Kotsis V, Toumanidis S, Papamichael C, Constantopoulos A, Zakopoulos N. White-coat and masked hypertension in children: association with target-organ damage. Pediatr Nephrol. 2005; 20: 1151-1155.
25. Lurbe E, Torro I, Alvarez V, et al. Prevalence, persistence, and clinical significance of masked hypertension in youth. Hypertension. 2005; 45: 493-498.
26. Wühl E, Witte K, Soergel M, Mehls O, Schaefer F. Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions. J Hypertens. 2002; 20: 1995-2007.
27. Stergiou GS, Karpettas N, Kapoyiannis A, Stefanidis CJ, Vazeou A. Home blood pressure monitoring in children and adolescents: a systematic review. J Hypertens. 2009; 27: 1941-1947.
28. Woroniecki RP, Flynn JT. How are hypertensive children evaluated and managed? A survey of North American pediatric nephrologists. Pediatr Nephrol. 2005; 20: 791-797.
29. Stergiou GS, Nasothimiou E, Giovas P, Kapoyiannis A, Vazeou A. Diagnosis of hypertension in children and adolescents based on home versus ambulatory blood pressure monitoring. J Hypertens. 2008; 26: 1556-1562.
30. Stergiou GS, Rarra VC, Yiannes NG. Prevalence and predictors of masked hypertension detected by home blood pressure monitoring in children and adolescents: the Arsakeion School study. Am J Hypertens. 2009; 22: 520-524.
31. Stabouli S, Kotsis V, Zakopoulos N. Ambulatory blood pressure monitoring and target organ damage in pediatrics. J Hypertens. 2007; 25: 1979-1986.
32. Wühl E, Trivelli A, Picca S, et al. Strict blood-pressure control and progression of renal failure in children. N Engl J Med. 2009; 361: 1639-1650.
33. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol. 1986; 57: 450-458.
34. de Simone G, Daniels SR, Devereux RB, et al. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. J Am Coll Cardiol. 1992; 20: 1251-1260.
35. Daniels SR, Witt SA, Glascock B, Khoury PR, Kimball TR. Left atrial size in children with hypertension: the influence of obesity, blood pressure, and left ventricular mass. J Pediatr. 2002; 141: 186-190.
36. Daniels SR, Loggie JM, Khoury P, Kimball TR. Left ventricular geometry and severe left ventricular hypertrophy in children and adolescents with essential hypertension. Circulation. 1998; 97: 1907-1911.
37. Simonetti GD, Schwertz R, Klett M, Hoffmann GF, Schaefer F, Wühl E. Determinants of blood pressure in preschool children: the role of parental smoking. Circulation. 2011; 123: 292-298.
38. Meyers RS, Siu A. Pharmacotherapy review of chronic pediatric hypertension. Clin Ther. 2011; 33: 1331-1356.
39. Pappadis SL, Somers MJ. Hypertension in adolescents: a review of diagnosis and management. Curr Opin Pediatr. 2003; 15: 370-378.
40. 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: 2489-2499.
41. Simonetti GD, Rizzi M, Donadini R, Bianchetti MG. Effects of antihypertensive drugs on blood pressure and proteinuria in childhood. J Hypertens. 2007; 25: 2370-2376.
42. Mattoo TK, Treatment of hypertension in children and adolescents. Editors Stapleton FB, Kim MS. UpToDate, Inc. Wolters Kluwer, Waltham, MA, US. Available at http://www.uptodate.com/contents/treatment-of-hypertension-in-children-and-adolescents. Accessed 24 July 2012.
43. Kotchen JM, Holley J, Kotchen TA. Treatment of high blood pressure in the young. Semin Nephrol. 1989; 9: 296-303.
44. Sinaiko AR. Treatment of hypertension in children. Pediatr Nephrol. 1994; 8: 603-609.
45. Wells TG. Trials of antihypertensive therapies in children. Blood Press Monit. 1999; 4: 189-192.
46. Robinson RF, Nahata MC, Batisky DL, Mahan JD. Pharmacologic treatment of chronic pediatric hypertension. Paediatr Drugs. 2005; 7: 27-40.
47. Raes A, Malfait F, Van Aken S, France A, Donckerwolcke R, Vande Walle J. Lisinopril in paediatric medicine: a retrospective chart review of long-term treatment in children. J Renin Angiotensin Aldosterone Syst. 2007; 8: 3-12.
48. Li JS, Baker-Smith CM, Smith PB, et al. Racial differences in blood pressure response to angiotensin-converting enzyme inhibitors in children: a meta-analysis. Clin Pharmacol Ther. 2008; 84: 315-319.
49. Simonetti GD, Rizzi M, Donadini R, Bianchetti MG. Effects of antihypertensive drugs on blood pressure and proteinuria in childhood. J Hypertens. 2007; 25: 2370-2376.
50. Herder SD, Weber E, Winkemann A, Herder C, Morck H. Efficacy and safety of angiotensin II receptor type 1 antagonists in children and adolescents. Pediatr Nephrol. 2010; 25: 801-811.
51. Sahney S. A review of calcium channel antagonists in the treatment of pediatric hypertension. Paediatr Drugs. 2006; 8: 357-373.